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A PRELIMINARY REPORT ON THE ADVANTAGES OF A SMALL STOMA IN PARTIAL GASTRECTOMY FOR ULCER*

By H. W. Porter and Z. B. Claman

Edinburgh, Scotland

In the treatment of chronic peptic ulceration, it is now generally accepted that partial gastrectomy consistently gives the most satisfactory results. Although the results on the whole have been satisfactory, inasmuch as the predominant symptom—pain—has been relieved and the chances of stomal ulceration greatly reduced, there is no doubt that gastrectomy has often left the patient with other less severe disabilities. We feel that many of these can be almost completely eliminated by a minor modification in the type of operation carried out.

Clavel[5] and many others believe that the most physiological type of gastrectomy is the Hofmeister-Finsterer operation. This operation has certain advantages attributable to the valve which is made to prevent regurgitation of food into the duodenum.

Many believe that the size of the stoma has no effect on the final results of the operation and this assumption is largely based on the experimental work of Mehring and McCann.[8]

Hofmeister recognized the danger of leakage occurring at the upper angle of the anastomosis of a full length gastro-jejunal stoma after sub-total gastrectomy, and in order to avoid this leakage and thus reduce his mortality rate, he advised the infolding of the upper end of the gastric remnant for 2 or 3 cms.

Finsterer[2] made the observation that unpleasant symptoms after gastrectomy often occurred as a result of the reflux of gastric contents into the afferent jejunal loop. Wright[3] in 1929, described two cases where barium could be seen entering the proximal duodenal loop, and both these cases complained of discomfort. Ogilvie[4] in 1947, stated that this reflux is the commonest cause of postoperative discomfort. Finsterer's early recognition of this cause of postoperative discomfort led him to advocate the closure of the upper part of the gastric remnant, so as to leave 10 cms. of the lower end open. The valve so formed was intended to prevent reflux into the afferent loop, in addition to making the anastomosis safer from leakage.

One of the authors (P) undertook to make the stoma much smaller than is usual in order to increase the emptying time.

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Since emptying time appears to have direct bearing on the clinical end results, as shown by Strauss[6] and others, we have carried out a series of cases making the stoma much smaller than is usual in an endeavour to delay emptying time. Mehring in 1897, from experimental work with dogs, concluded that the pyloric sphincter does not control the emptying time of the stomach, and after its removal the emptying time of the remnant is the same as that of the intact stomach. Since then, others have repeated his experimental work, and confirmed his results. McCann[8] 1939, repeated this experiment and came to the same conclusions but added the important fact that the quantitative emptying time is definitely affected, and showed that although the total emptying time remains the same after the removal of the pyloric sphincter, the quantitative emptying time is reduced. In other words, the volume of the gastric residue 30 minutes after a meal in the resected stomach, is much less than that in the intact stomach. This latter observation appears to have been ignored by most writers on the subject, with few exceptions. Shay and Gershon-Cohen[9] recognized this factor, making a clear differentiation between the total emptying time, in which the pyloric sphincter plays very little part, and the quantitative emptying time, in which the sphincter plays a definite role. Thus theoretically, if a sphincteric-like action could be obtained at the gastrojejunal stoma, the likelihood of a delayed quantitative emptying time should be increased, although the total emptying time might remain unaffected.

McCann[8] from experimental work on dogs in which he resected increasing amounts of stomach, connecting the gastric remnant to the small intestine, came to the conclusion that the size of the stoma had no relation to the emptying time of the gastric remnant. Ravdin[11] and others came to the conclusion that the new stoma, regardless of size, is not the reason for the rapid gastric emptying. By these statements, various writers in the literature have confirmed the impression that the size of the stoma will not control the emptying time of the gastric remnant. Recently Kennedy, Reynolds and Cantor[12] have pointed out that the factor which controls emptying time of the stomach is not the size of the stoma but the size of the jejunal lumen. This, however, only applies when the size of the stoma is greater than the size of the jejunum, and also presumes that the stoma has no sphincteric action.

Recognizing these facts, we have made a stoma 2.5 cm. in length in a series of 118 sub-total gastrectomies for ulcer. The indications for operation have been:

Repeated Perforations—				
1	— 30 cases			
2	— 7 cases			
4	— 1 case	—	38	
Hemorrhage—				
Acute Massive	— 8 cases			
Multiple	— 9 cases	—	17	
Failed Medical Treatment		—	63	118

and we have found the following advantages:

(1) *The advantages of the Hofmeister-Finsterer Valve.*
   (a) Decreased incidence of leakage at the upper end of the anastomosis.
   (b) Decreased incidence of retrograde influx into the proximal jejunal loop.
(2) *Bulging of the jejunum after food is prevented.*

FIG. 1.—A. X-ray showing the bulging of the jejunum (J) opposite the wide anastomosis after a Polya gastrectomy.

Kennedy, Reynolds and Cantor,[12] in a review of 90 cases of Polya type of gastrectomy, found a uniform roentgen ray finding of jejunal dilatation and show a post-mortem specimen drawing, which clearly indicates the jejunal dilatation that occurs with the wide gastro-jejunal type of stoma. (Fig. 1). They say that this jejunal bulge prevents the patient from eating a normal volume of food and is one of the causes of postprandial discomfort—with this we are in full agreement. This tendency to bulging was also recognized by Vitkin,[7] Gordon Taylor[13] and others. In our series, where 90 cases have been followed up radiologically, there was no jejunal bulge in 84 cases, and only slight fullness in six. In no instance was the jejunal bulge present to the degree indicated by Kennedy[12] *et al.*

(3) *The risk of postoperative hemorrhage is diminished.*

The source of hemorrhage after gastrectomy is from the cut edges of jejunum and stomach. As the jejunum is only incised for a length of 2½ cms. the risk of hemorrhage is correspondingly reduced. Allan and Welch[14] in a series of 151 cases of gastrectomy with long stomas reported four fatal hemorrhages. Reinhoff[15] reports 10 per cent of hemorrhage (non-fatal and fatal) occurring after a Polya type gastrectomy in 260 cases. In this series of 118 cases, there has been no case of serious hemorrhage from the stoma; six cases had slight hemorrhage but these improved with conservative treatment.

(4) *Increased emptying time.*

The normal stomach empties in 3½–4 hours using a water barium sulphate mixture. It has been shown by Ravdin[11] that varying the solution will affect the emptying time. Vitkin[7] states that the average emptying time after gastrectomy is 20 minutes, and quotes various European authors who point out that the emptying time may be much less. Shay and Gershon-Cohen[9] believe that the decrease in emptying time following gastrectomy is the direct result of achlorhydria. They show that in no cases of gastric resection does the emptying time exceed 30 minutes. Gilbert and Dunlop[16] say that it is a well established fact that the gastric remnant empties quickly and that the rate of emptying is increased following a carbohydrate meal. It is interesting to note that the intact achlorhydric stomach empties in 15–90 minutes. Strauss[6] and others reported 25 cases of gastrectomy in which 25 per cent emptied in 15–20 minutes. They state that the slower the emptying time, the better is the clinical end result. It must be noted, however, that the total emptying time was used; no estimation of quantitative emptying time was made.

FIG. 1. — B. Line drawing showing the bulging of the jejunum (J) opposite the wide anastomosis after a Polya gastrectomy.

Quantitative emptying time may be defined as the period taken for the fluid level in the gastric remnant to disappear after a barium meal. Flakes of barium which may be seen adhering to the mucosa after a meal, are disregarded.

In this series in which 40 cases were followed, the average quantitative emptying time was 58 minutes. Only three cases in this series had quantitative emptying time of less than 30 minutes. Two of these cases were followed up one month after operation and the remaining case one year after operation. Eight cases had an emptying time of 30–40 minutes and the remaining 29 cases had an emptying time exceeding 45 minutes. Of these, five cases were followed up less than six weeks after operation and five cases less than three months.

(5) *Sphincteric-like action of the stoma.*

Schindler[17] on following up 52 cases of a Polya type gastrectomy, found that on gastroscopic examination, 48 of the cases had a rigid type of stoma which remained patent throughout. In these cases there was considerable edema with inflammatory change and erosion of the gastric and jejunal mucosa. In only four cases was there a sphincteric-like action at the stoma and these four cases were the only ones with a healthy mucosa and which were

entirely symptom free. We think that the sphincteric-like action is due to contractions of the jejunal musculature rather than that of the stomach, as the first swallow of barium passes straight through the stomach into the jejunum (Fig. 2A) which then contracts and closes the stoma. The stomach then fills (Fig. 2B) and as the jejunum, having emptied, relaxes, more barium flows through the stoma. In 88 per cent of the cases in our series there was roentgenologic evidence of this sphincteric-like action, which usually appeared within six weeks of operation.

The prevention of jejunal bulging and the increased emptying time encourage the early resumption of a normal diet postoperatively. The psychologic effect of a diet, normal in quantity, cannot be over-emphasized. In this series, fluids—milk or sweetened drinks—were given within 12 hours of operation, and within 10 days the patients were receiving a normal hospital diet. This has an important effect in convincing the patient that he has now a healthy stomach. The patient leaves hospital with specific instructions to eat and drink anything he wishes. The vast majority of our patients have been ready to follow these instructions. Of the 112 patients followed, all except two have returned to their former employment, these two having been off work for 15 years before operation. We have also found that weight gain is much more rapid if a normal diet is returned to at an early date, and that there is a very low incidence of post-gastrectomy anemia. If a wide stoma is used, it is generally accepted that frequent small meals and prolonged postoperative medical care with a comprehensive but concentrated diet are desirable. With a small stoma, this careful postoperative care is eliminated.

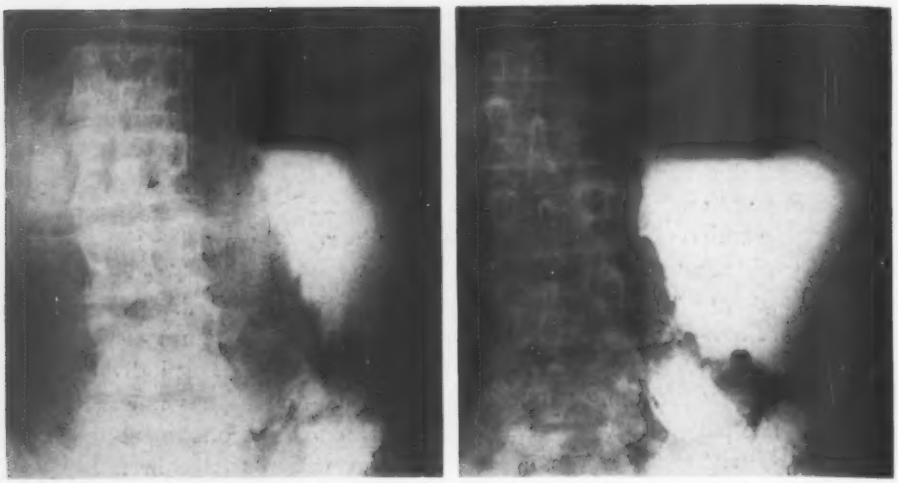
The reasons for these advantages are:

(a) The stoma functions immediately. (Fig. 3).

We have several roentgenograms taken between 12 and 24 hours after operation which show the passage of barium through the stoma. Allan and Welch[14] record eight cases of obstruction with a full length stoma in a series of 151 cases. In our series there has been one case.

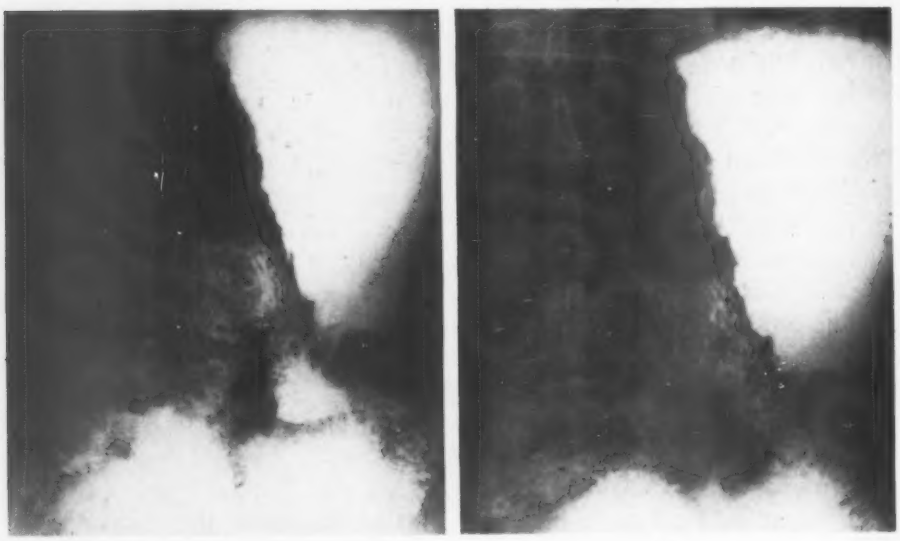
(b) With the early sphincteric-like action of the stoma, there is rapid dilatation of the gastric remnant and delayed emptying time. This was shown in 60 cases, x-rayed 4–6 weeks after operation, in which the gastric remnant had the capacity approximating that of a normal stomach. Vitkin[7], who reviewed 45 cases with wide stomas, found that in the first three months six had an average sized gastric remnant and in all of the remainder the gastric remnant was high and small. Strauss[6] *et al.*, discussing the size of the gastric remnant after resection of two-thirds of the stomach, observed that 69 per cent of the remnants remained the same size, 17 per cent decreased and 14 per cent increased in size, and made the statement that the slower the emptying time the better the clinical end results. In 13.2 per cent of the cases in our series the gastric remnant remained the same size and in 86.8 per cent the size was increased. None of the cases showed decrease in size.

(c) Another asset of the small stoma is that it prevents jejunitis by protecting the jejunum from immediate contact with food over a wide surface. Schindler[17] demonstrated jejunitis in 92 per cent of the cases which he exam-



A B

FIG. 2.—X-ray appearance six weeks after a gastrectomy using a small stoma. It will be noticed in (C) and (D) that there is barium in the proximal loop, this has been pushed back by the radiologist. (A) The barium is seen to run straight through the stoma and into the jejunum after taking the first swallow. (B) Some seconds later the stoma is seen to close and the stomach fills and distends. Note the size and the level of the air bubble.



C D

FIG. 2.—(C) The stoma is open and the barium is seen flowing into the jejunum. Peristalsis is taking place in the stomach as shown by the size and the level of the air bubble. (D) The stoma is closed and the stomach is undergoing peristalsis.

ined with the gastroscope. Vitkin[7] believed that out of a series of 132 cases with full length stoma all had a chronic jejunitis, with the exception of five patients where improvement was observed; it persisted in the remaining 127 cases for years. This is responsible for vague abdominal discomfort often not complained of but tolerated by many patients. In our series of 80 cases, followed up radiologically, only one had definite evidence of jejunitis.

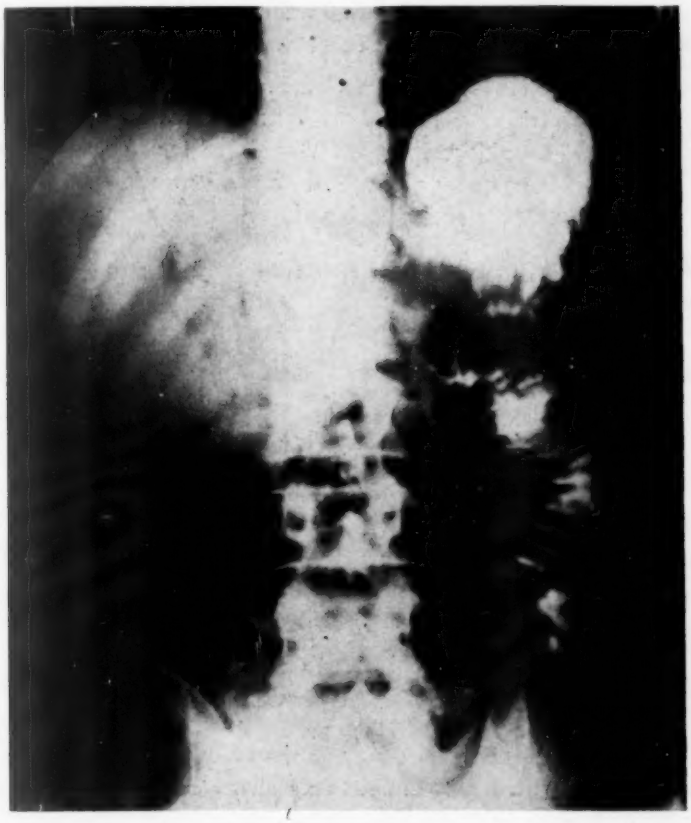


FIG. 3.—Barium meal 20 hours after a gastrectomy using the small stoma and showing the barium passing into the jejunum. Note the position of the esophagus indicating the level of the resection and the size of the remnant before dilatation has occurred.

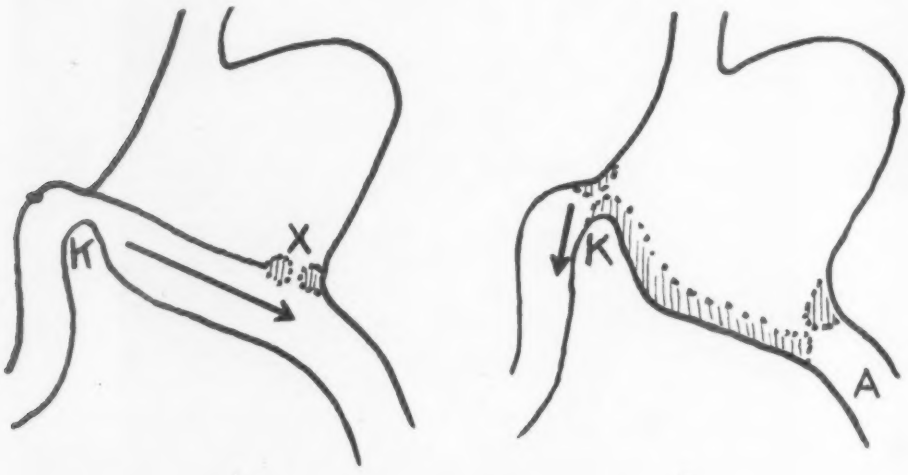
(d) Leakage at the duodenal stump may be due to faulty closure but we are of the same opinion as Alleson[19] and Tintel[20] that the commonest cause is obstruction of the proximal loop at the site of anastomosis preventing the passage of the normal duodenal and pancreatic secretions (1500 cc. daily). This obstruction may be caused either by kinking at the upper part of the anastomosis or by edema—producing a temporary paralysis of the proximal jejunum.

With a small stoma, the amount of edema is minimal and if the jejunum is stitched to the closed upper part of the gastric remnant, edema and kinking cannot occur at the same place. Slight kinking or edema in themselves may not

be sufficient to cause obstruction but when they occur together, complete obstruction may be precipitated. (Fig. 4).

In the 118 instances in which we have used a small stoma these points have been substantiated. There has been no case of leakage of the duodenal stump and in only nine cases has postoperative gastric suction been necessary.

Seven of these cases had slight postoperative hemorrhage. In one, there was an organic small bowel obstruction for which further operation was necessary on the fifth day, when a loop of small bowel adherent to the inside of the wound, was separated, after which convalescence was uneventful. In one case, the



A B

FIG. 4.—(A) Line drawing of a small stoma gastrectomy indicating the sites where edema (X) and kinking (K) may occur, but their positions are held apart.

(B) Line drawing of a large stoma gastrectomy indicating edema and kinking may occur at the same site.

stoma was made too small (1.5 cm.). This also necessitated re-operation on the fifth day, with enlargement of the stoma. It is interesting to note that in this case the small gastric remnant had distended to 40 ozs. on the second postoperative day before suction was instituted, without any ill effects.

DUMPING

The dumping syndrome, as defined by Custer, Butt and Waugh[21] of the Mayo Clinic, consists of four cardinal and almost invariable symptoms occurring 15–30 minutes after food.

They are:

(1) Profound nausea and weakness.
(2) Generalised unpleasant feeling of warmth.
(3) A cold sweat especially of the forehead and face.
(4) Palpitation.

The cause of this syndrome is still debatable. There are three possibilities:

1. Sudden distention of the jejunum. While sudden jejunal distention does cause a feeling of fullness immediately after food is swallowed and is exceedingly common after operations of the Polya wide stoma type, it cannot be regarded as the primary cause of dumping because when levulose is used in place of dextrose to distend the jejunum, the flushing, sweating and lassitude do not appear.

2. Jejunitis. It has been observed that the majority of cases with the dumping syndrome show radiologic evidence of jejunitis but this may be in itself the result of too rapid emptying. In those cases in this series which have exhibited the syndrome, there has been no evidence of jejunitis.

3. Hypoglycemia. It has been recognized for a considerable time that after gastrectomy or gastro-enterostomy, carbohydrates are more rapidly absorbed than usual.

This rapid absorption results in an over-stimulation of the production of insulin which in turn leads to a sudden drop of blood sugar level and results in hypoglycemia 1–1½ hours after food. Severe hypoglycemia may induce the excessive secretion of adrenalin which may simulate in every respect the dumping syndrome.

Since, however, the dumping symptoms usually occur within half an hour after food, it will be seen that there is some room for doubt as to the validity of this theory. It may be, however, that the rate of fall in blood sugar level from hyper- to hypoglycemia is associated with the upset.

The one constant feature which is present in all these theories is too rapid emptying of the stomach.

Gilbert and Dunlop[16] reported that 35 per cent of patients who had had gastrectomy of various types carried out presented the dumping syndrome.

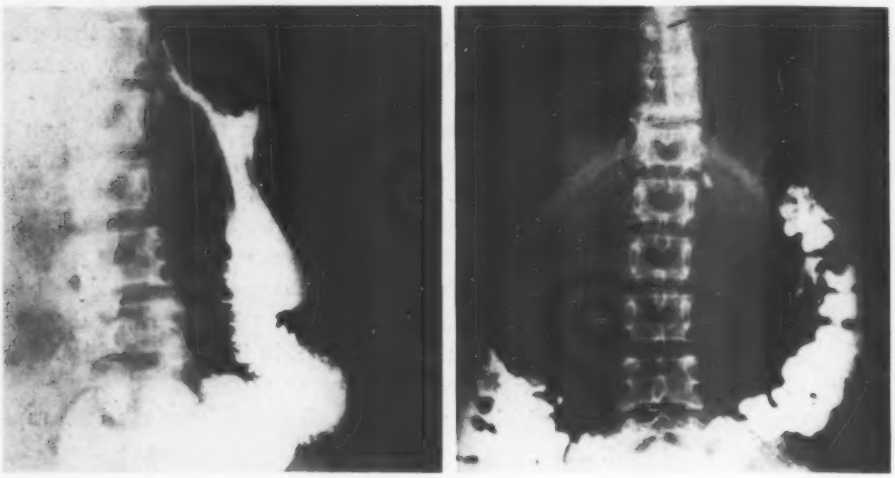
In this series, there have been 17 patients (15 per cent) from whom the history of the dumping syndrome could be elicited by asking leading questions. Twelve of these patients were symptom free within three months of operation. Of the remaining five, three have only had a three months' follow-up and are improving; in one case the syndrome has persisted for two years; and in one case for one year. Both of these, however, are able to work. We think these figures compare very favorably with those to be found in Gilbert and Dunlop's[16] series in which 10 per cent of their gastrectomy patients were unfit for any form of employment because of the dumping syndrome.

It is interesting to note that a number of patients who presented themselves for operation had symptoms identical with the dumping syndrome preoperatively. All except the five already referred to have completely cleared up after operation. It has been found by Abrahamson[23] that patients suffering from duodenal ulcer have a low blood sugar level. This is an interesting observation which we hope to investigate further.

It is probable that the small incidence of persistent dumping in this series is due to the delayed emptying time of the gastric remnant due to the early development of a sphincteric-like action of the small stoma.

While many people believe that the size of the stoma has no influence on the emptying rate and that this is controlled only by the size of the lumen of the jejunum, this view is not borne out by our experience. Forty cases have had a follow-through barium series and the average time taken for the stomach to empty has been 58 minutes. That is the time taken for the fluid level in the stomach to disappear as opposed to 15–20 minutes in patients who have had a full length anastomosis performed.

This delayed emptying time is not due to any organic obstruction as during the first few days barium flows straight through into the jejunum and the



A B

FIG. 5.—Barium meal 18 months after a Polya full length stoma gastrectomy. (A) Immediately after meal showing very rapid emptying of the stomach and jejunal bulging. (B) One hour after meal showing the stomach and small bowel completely empty.

stomach empties rapidly. The majority, however, have developed delay and sphincteric-like action within six weeks.

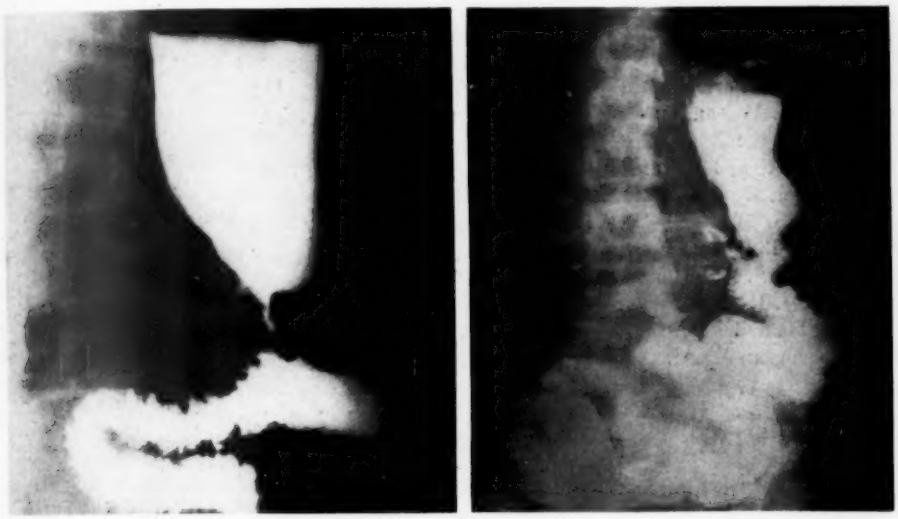
In addition we have recently had a patient who had had a full length Polya type gastrectomy carried out 18 months previously with such severe postprandial dumping symptoms that it was necessary for her to lie down for one hour after every meal: She was also afraid to eat in a public place for fear of fainting. Accordingly a second operation was performed and the size of the stoma was reduced to 2½ cms. The patient's symptoms were completely relieved by this operation and within 14 days she was able to take a full normal diet. A barium meal on the 11th day showed sphincteric-like action of the stoma and emptying time of over one hour. (Fig. 5). Three months later this patient had gained 10 lbs. in weight and appeared to be in perfect health.

Arguments against the use of the small stoma are as follows:

(1) It may be said that regurgitation of alkaline juices into the gastric

remnant with neutralization of any remaining free hydrochloric acid is prevented, but it is now generally accepted that if the resection has been adequate, stomal ulceration is exceedingly rare. In any case, most recurrent ulcers are jejunal and not gastric.

(2) Obstruction might occur later at the site of the stoma. We have followed some of these patients for over five years and we have had no single case of delayed postoperative vomiting or any evidence of late stenosis.



C D

FIG. 5.—(C) Barium meal 11 days after a reconstructive operation on the stoma reducing its size to 2½ cms. Lateral x-ray 5 minutes after the meal.

(D) One hour after the barium meal.

CONCLUSIONS

Evidence is produced from a series of 118 partial gastrectomies for peptic ulcer to show that a stoma of 2.5 cm. long has the following advantages:

(1) The small stoma with a Hofmeister-Finsterer valve reduces the risk of incidence of—
  (a) leakage at the duodenal stump.
  (b) leakage at the anastomosis.
  (c) postoperative hemorrhage from the anastomosis.
  (d) the necessity for routine postoperative suction.
  (e) jejunitis.

(2) The small stoma encourages—
  (a) sphincteric action at the stoma.
  (b) delayed emptying time.
  (c) the ability to eat a full normal diet at an early date, shortening convalescence.

(3) The small stoma reduces the incidence of the dumping syndrome.

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THE OPERATIVE TREATMENT OF PECTUS EXCAVATUM*

MARK M. RAVITCH, M.D.

BALTIMORE, MD.

FROM THE DEPARTMENT OF SURGERY, THE JOHNS HOPKINS UNIVERSITY AND THE JOHNS HOPKINS HOSPITAL, BALTIMORE, MARYLAND

THE OPERATION FOR PECTUS excavatum was put in proper perspective by the detailed review of Ochsner and DeBakey[1] in 1939 and by the series of patients presented by Lincoln Brown[2] in the following year. Since the recent publications of Sweet[3] and of Lester[4] with their modifications of previous technics, pectus excavatum has been established even more firmly as a congenital deformity amenable to surgical correction.

Pectus excavatum (funnel breast, Trichterbrust) is a deformity of the thorax marked by a sharp posterior curve of the body of the sternum, deepest just before its junction with the xiphoid. The lower costal cartilages bend inward to form a depression, the lateral borders of which are angled more sharply than the superior and inferior portions. A paradoxical inward motion of the lower sternum is conspicuous on inspiration. The deformity is present at birth and usually is progressive. The chest becomes flat and thin, the dorsal spine kyphotic, the head thrust forward. In extreme instances the deepest portion of the concavity to one side of the midline may be posterior to the ventral surface of the vertebral bodies. In the undressed patient the concavity is conspicuous and unsightly and a source of embarrassment to young individuals of either sex. The deformity of rib cage and spine in the more severe instances is quite plain even when the patient is clothed. Physiologic disturbances may occur due to displacement of the heart or pressure upon it, but this is usually delayed until adolescence or later. There have been numerous reports of dyspnea and cardiac arrhythmias, such as paroxysmal tachycardia; their occurrence is not necessarily confined to the patients with the most severe deformities. It seems likely, however, that the dyspnea in the adult with shallow, rigid chest is on a pulmonary as well as a cardiac basis.

It is impossible to predict in which children the deformity will progress, since the mechanism of its production is still uncertain. The paradoxical depression of the sternum with each inspiration suggests that a short central tendon of the diaphragm might be responsible. Moreover, at operation one usually finds a tough fascial band tensely stretched between linea alba and sternum, the so-called substernal ligament. When this is divided the sternum may be elevated slightly without division of costal cartilages. On the other hand, the defect is generally obvious at birth and it seems unlikely that it has been produced solely by the pull of the diaphragm during fetal respiration.

It has been our feeling that operation should be undertaken in the more severe instances to correct the existing deformity and to prevent its progression. The younger the patient at the time of correction, the more favorable are

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his chances for attaining a normal appearance with subsequent growth of the thoracic cage.

The indications for operation are (1) cosmetic, (2) orthopedic, and (3) physiologic:

(1) The deformity itself is a source of concern to children and parents and a basis for teasing by playmates. The extent to which this has disturbed a

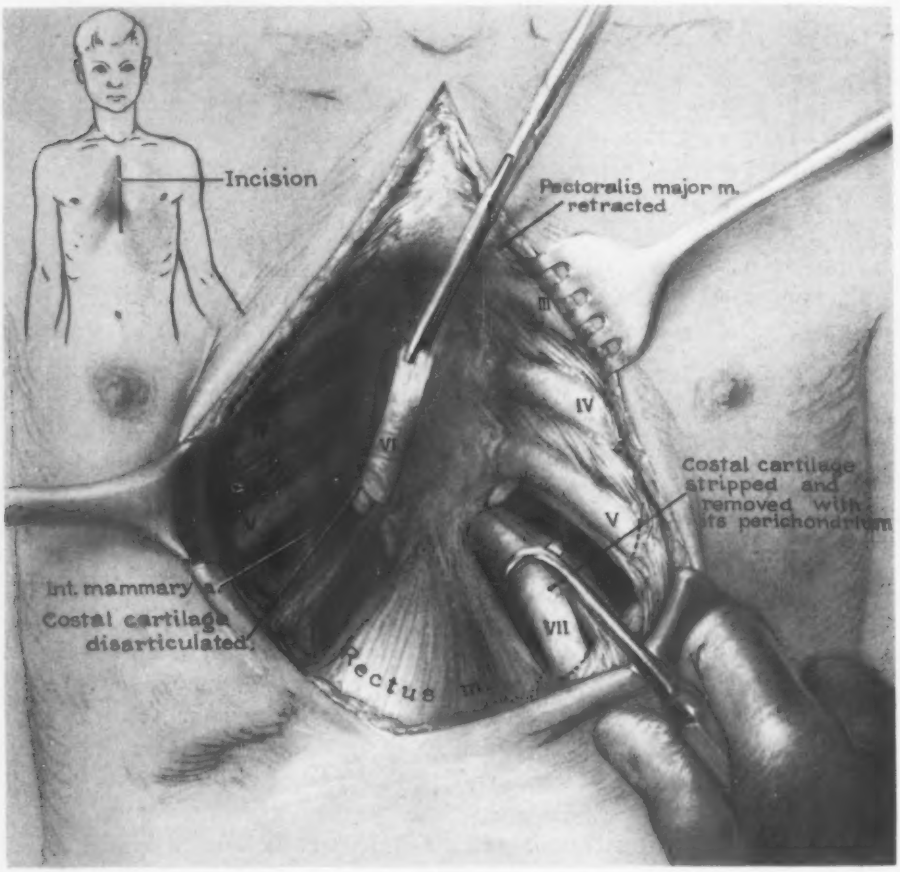


FIG. 1.—Midline incision from manubrium to epigastrium. The pectoral muscles are stripped back and the costal cartilages resected together with the perichondrium. The entire deformed segment of each involved cartilage is resected.

patient and his family is usually fully appreciated only after the operation. The correction of the defect seems to permit patient and family alike to discuss freely what had previously been minimized by a protective reticence.

(2) The antero-posterior flattening of the chest and the kyphosis will gradually disappear, if operation is performed early enough. As indicated hereafter, prophylaxis is better than cure.

(3) If dyspnea, exercise intolerance, or cardiac arrhythmias are present, operation is strongly indicated.

In children with pronounced defects, operation should be undertaken before there is any marked general thoracic deformity and before physiologic disturbances occur. One cannot predict which children will suffer most, if not operated upon. On the other hand, one may say that a less formidable operation in infancy will probably ensure normal development, whereas a more extensive operation some years later may secure only a partial correction of the deformity.

The procedure we have employed differs in some respects from those reported. It is designed to prevent any further deformity and to correct the existing deformity. For this reason we have felt it necessary to divide the xiphi-sternal articulation and substernal ligament and to resect all the deformed

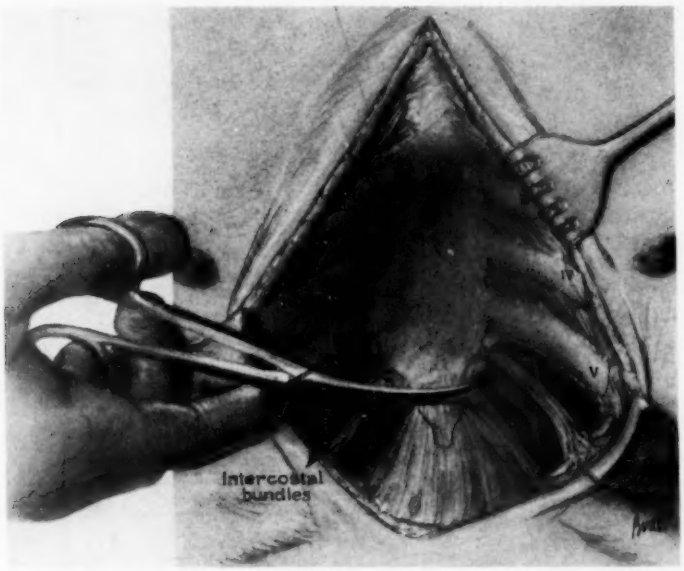


FIG. 2.—The two lowermost costal cartilages on each side have been resected, giving access to the xiphoid. The xiphi-sternal articulation is divided.

costal cartilages for the length of their deformity. The usual transverse cuneiform osteotomy is performed at the sterno-manubrial junction and the corrected position maintained by braided silk sutures. No traction apparatus is employed. The extensive defect resulting from excision of all of the deformed cartilage makes it impossible to suture the remaining cartilage ends to the sternum. No cast or other apparatus is employed to support the chest.

Technic: Under intratracheal ether anesthesia a midline incision is made from manubrium to epigastrium. The upward rise of the xiphoid and epigastrium from the sternal hollow is often nearly vertical and the sharp declivity makes it difficult to work in this area. In infants and small children it is relatively easy to strip the pectoral muscles from the sternum, exposing the costal cartilages. With the periosteal elevator all of the deformed cartilages are

exposed for the full extent of their deformity. The two lowermost cartilages on each side are divided at the lateral edge of the deformity and are then disarticulated from the sternum (Fig. 1). In infants and children it is exceedingly difficult to perform subperichondral resection and no attempt is made to preserve the perichondrium. The deformity is such that the lowermost cartilages on each side usually lie together like the ribs of a fan, hindering exposure of the xiphoid. Only after these cartilages have been resected is one readily able to expose and separate the xiphisternal junction. As the scissors open the

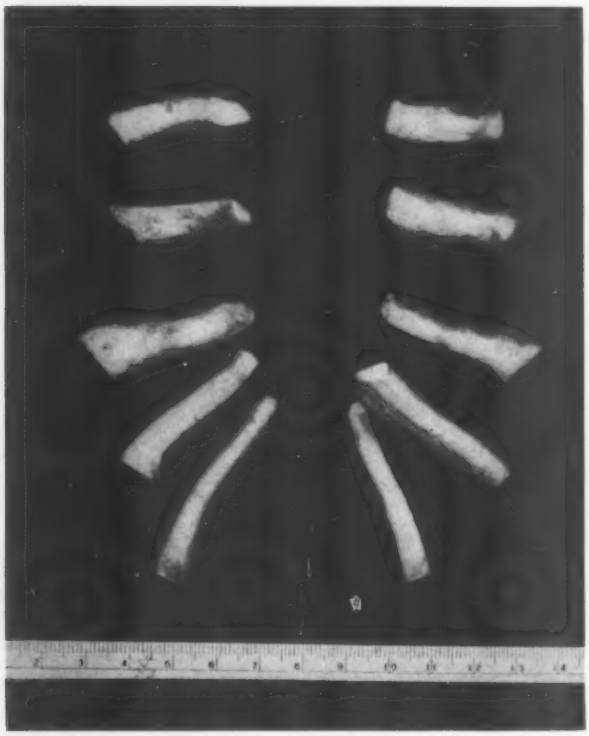


FIG. 3.—Segments of costal cartilages removed at operation on Patient M. K., Case 2. The full length of the malformed portion of each involved cartilage is removed. This patient was four years old and notice that the lower segments are almost five centimeters in length.

xiphisternal joint (Fig. 2), one can usually see the tough fibrous substernal ligament behind it. When this is divided the xiphoid pulls well away from the sternum—at times with an audible snap. Any remaining attachments of the rectus muscles to the sternum are divided. The finger can then be introduced into the mediastinum and the sternum freed of diaphragmatic attachments until the finger reaches freely to the manubrium. At this point one has completed what is essentially the "limited" operation of Brown. In one infant (Case No. 3) we had planned to do no more than this but found that there was still

a marked deformity and so continued the operation. The remainder of the deformed costal cartilages on both sides are then removed. The number varies with the severity of the deformity. We have taken from three to five cartilages on each side, resecting the full length of the deformed segment (Fig. 3). The intercostal structures are divided so that the body of the sternum is free except for its junction with the manubrium. A transverse cuneiform osteotomy (Fig. 4) is performed at the beginning of the downward curve in the sternum, cutting through to the posterior cortex. In the first two patients we employed an electric saw but now find osteotomes and an ordinary gouge to be simpler and more convenient. The sternum is then bent sharply anteriorly, fracturing

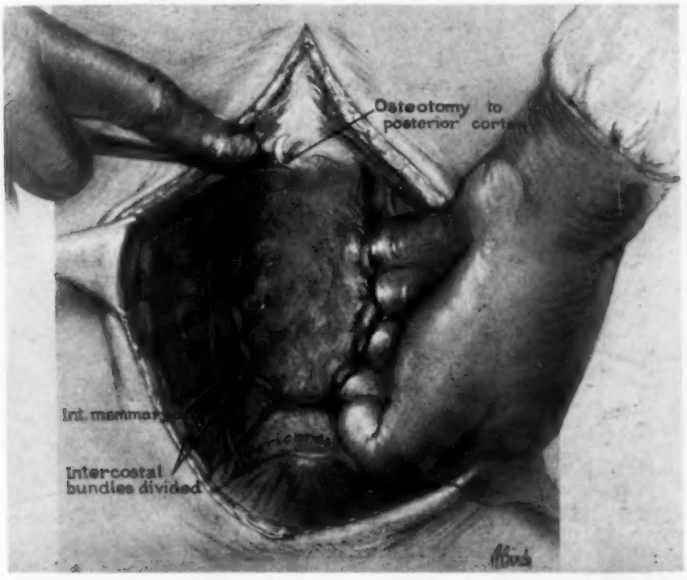


FIG. 4.—Five costal cartilages on each side have been resected and the corresponding intercostal bundles have been divided. The sternum is freed except at its upper end. With the gouge a transverse osteotomy is performed.

the posterior cortical lamella. Mattress sutures of braided silk are placed through the bone at the site of the osteotomy (Fig. 5) to secure the two portions of the sternum in a slightly over-corrected position. These sutures are reinforced by oo silk sutures placed in the periosteum. In the first two patients we used wires for external traction, but a fatal pyogenic infection in our second patient led us to abandon this technic, and we have seen no need to return to it. We have considered intramedullary fixation with a Kirschner wire, but in a recent adult patient with another type of sternal deformity, requiring two transverse osteotomies, sutures alone sufficed despite a heavy bony structure. Since the resected segments of cartilage are 3–5 cms. in length, we have considered it unwise to suture the remaining cartilage ends to the sternum. Despite this, the patients have not suffered from respiratory embarrassment. The

pectoral muscles are resutured (Fig. 6) to the edges of the superior portion of the sternum. All patients have received prophylactic blood transfusions from the outset of the operation. Of eight children operated upon, seven convalesced rapidly and may be considered excellent results. One child immediately after operation developed high fever and a massive wound suppuration which presently eroded the pleura and produced a fatal empyema. This child had bronchiectasis (as in Lincoln Brown's first patient), but the infection was most probably due to some gross break in technic in the operating room.

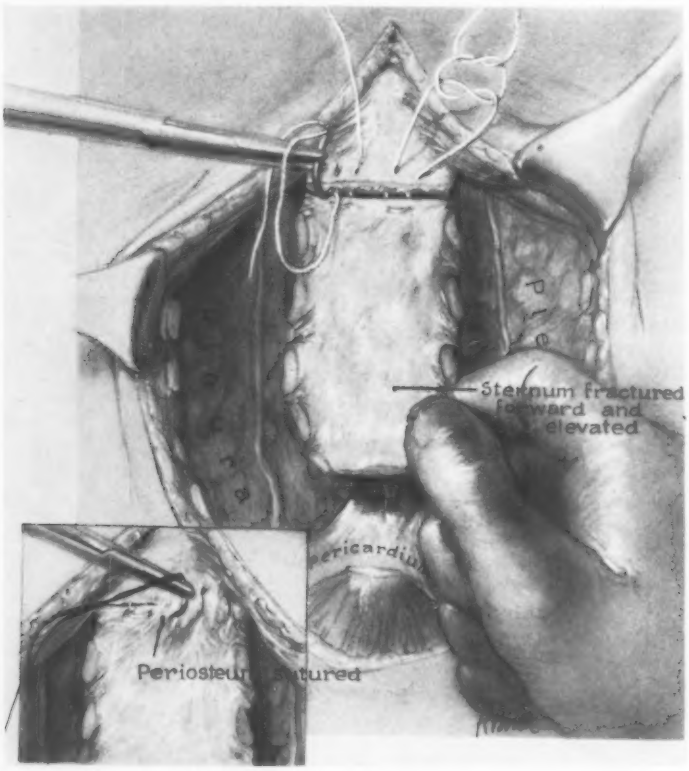


FIG. 5.—The sternum is elevated anteriorly, fracturing the posterior plate at the level of the osteotomy. The corrected position is maintained by mattress sutures of braided silk placed through the bone. The periosteum is then sutured with black silk.

CASE REPORTS

Case 1.—R. K., 409665. This was a thin, undernourished boy of 10. He had been noted at birth to have a "caved-in chest." His father was said to have the same deformity. It was thought that the boy's deformity had been increasing in severity. He had always been a "mouth breather," but no other cardio-respiratory symptoms had been noted. There was a marked funnel chest with a moderate degree of paradoxical respiration. The defect was long and narrow. His posture was poor with a forward thrust of the neck and a rounded dorsal spine.

On January 15, 1947, the five lowermost costal cartilages on each side were resected. A transverse osteotomy was performed in the sternum and sutured with silver wire. Traction was maintained on the sternum by wire sutures attached to a plaster cast. In two days he was out of bed. The traction apparatus was removed on the 15th day. On the 20th day measurements with obstetrical calipers showed that on inspiration the sternum moved outward a half centimeter instead of retracting one centimeter as before operation. He was last seen October 4, 1948. The improvement has been maintained.

Case 2.—M. K. A-51517. This was a boy 3 years and 9 months old who had been hospitalized repeatedly because of respiratory infections which had been diagnosed as pneumonia on several occasions. He had wheezed from birth. The sternal deformity was

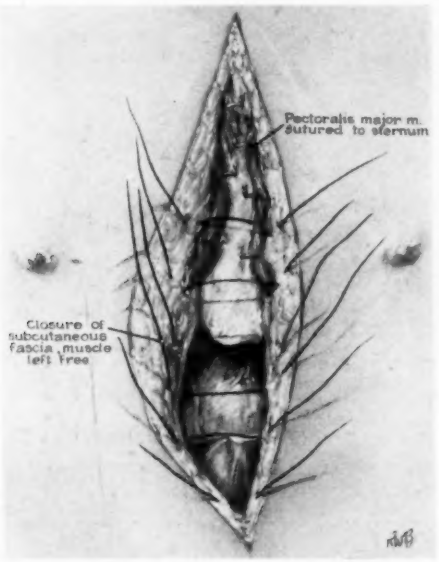
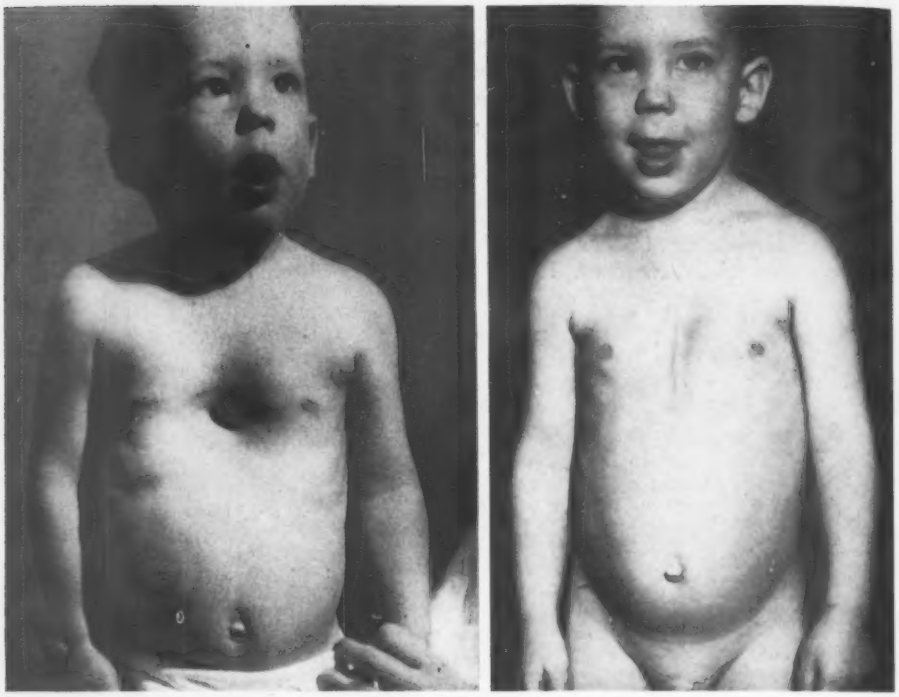


FIG. 6.—The pectoral muscles are sutured to the sternum in the upper portion. No attempt is made to replace the xiphoid or to re-attach the recti.

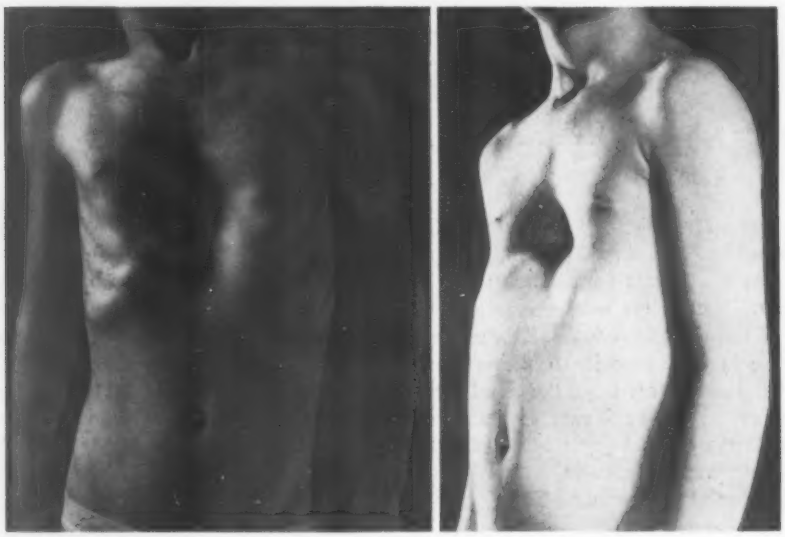
noted soon after birth. There was no family history of such a deformity. The child was malnourished and chronically ill. There was marked retraction of a deep sternal hollow and of the attached costal cartilages. He had a cough productive of whitish purulent sputum. There were rales everywhere over the lungs. Bronchograms showed bronchiectasis of the right lower lobe. It was decided that he would tolerate lobectomy better with increase in vital capacity resulting from correction of the pectus excavatum.

On January 21, 1947, the five lowermost costal cartilages on each side were resected from beyond the beginning of their curvature laterally to the sternum medially. The xiphoid was divided from the sternum and the substernal ligament divided. A wedge osteotomy was made with the electric saw and repaired with silver wire sutures, correcting the position of the sternum. Traction on the lower end of the sternum was made on a silver wire passing through the sternum and out through the skin, passing through a hole in a previously made plaster cast. On the third day after operation he developed a severe wound infection with hemolytic staphylococcus aureus. The wound broke down, empyema thoracis developed, and the child succumbed.



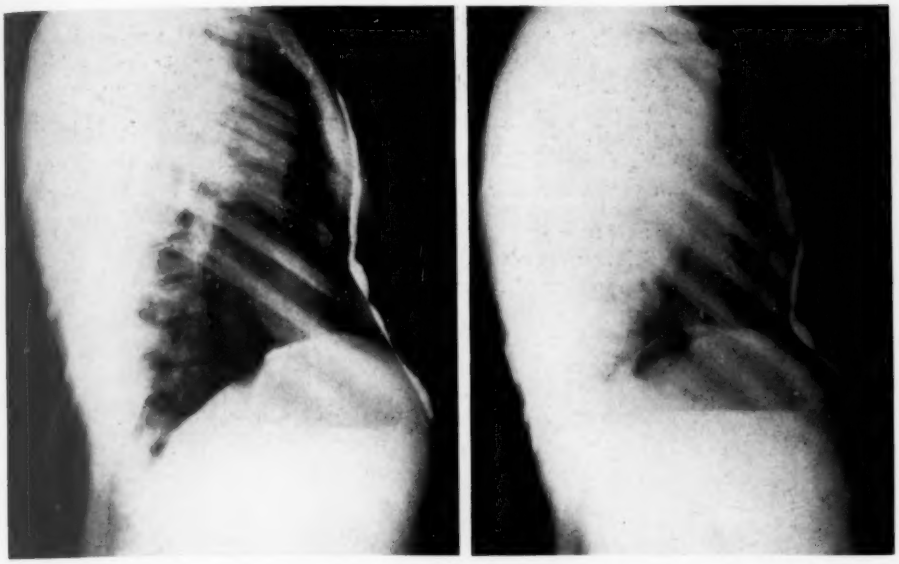
A B

FIG. 7.—Case 3. B. V., age 2 years. (A) Before operation. (B) Ten months after operation.



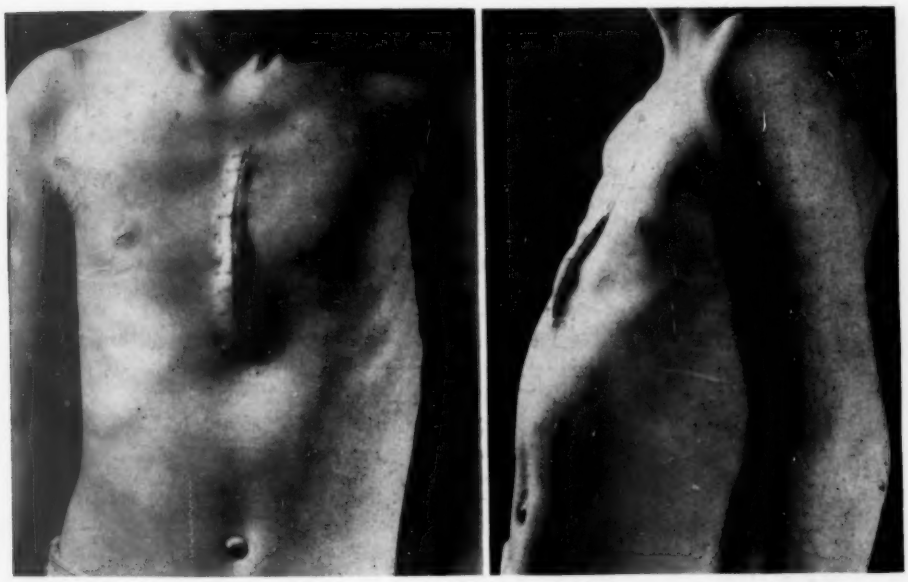
A B

FIG. 8.—Case 4.—R. E., age 7 years. (A & B) AP and oblique views before operation.



C D

FIG. 8.—(C & D) Preoperative lateral roentgenograms in expiration and inspiration. Note the marked change in contour and the paradoxical inward movement of the sternum on inspiration. A stripe of thick barium paste applied to the midline demonstrates the sternal contour.



E F

FIG. 8.—(E & F) AP and oblique views ten days after operation.

Case 3.—E. V., 420671. This was a 2-year-old boy whose development was retarded because of a birth injury. He had always been a "mouth breather" and had frequent upper respiratory infections. There was a deep round depression of his lower anterior chest which was thought to be increasing in severity (Fig. 7a). There was no familial history of such a deformity. There was prominent paradoxical movement of the incurved portion of the sternum. The child was vigorous and well nourished.

G

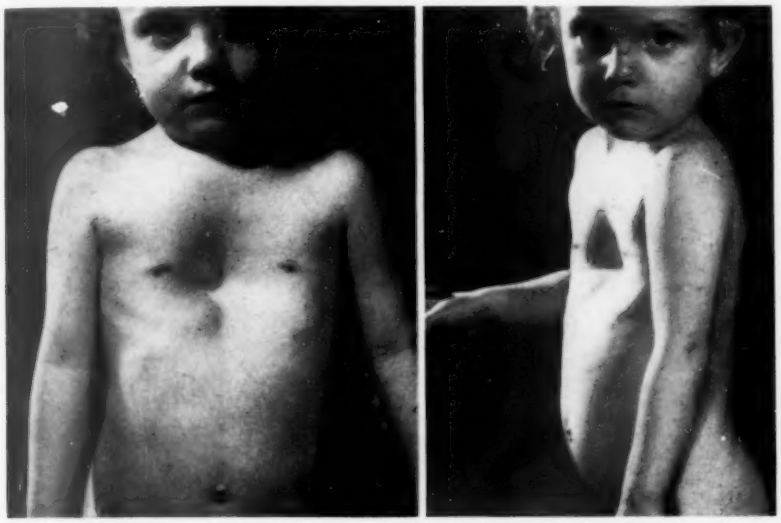
FIG. 8.—(G) Postoperative roentgenogram. The sternum is straight. The ridged cutaneous closure elevates the barium stripe. Roentgenograms taken in deep inspiration show the sternum equally straight and flat.

On May 15, 1947, operation was performed. It had been planned to do the "limited" operation, but resection of 3–4 cm. lengths of the 2 lowermost cartilages and separation of the xiphoid from the sternum with division of the substernal ligament failed to correct the deformity, although the paradoxical movement of the sternum ceased. Two more cartilages were, therefore, removed on each side. A transverse osteotomy was performed at the upper border of the defect, and the sternum was lifted anteriorly and held in place by a braided silk suture. He was sitting up and playing by the second day and was dis-

charged on the fourteenth day. Correction of the defect was satisfactory and has been maintained as seen in the photograph taken 10 months after operation (Fig. 7b).

Case 4.—R. E., 450812. (Fig. 8) This was a 7-year-old boy whose funnel chest was noted at birth. There was no familial history of such a defect. The boy was active and healthy, but was conscious of the defect which worried his parents and grandparents. The deformity was both wide and deep with pronounced paradoxical movement. There was no cardio-respiratory disability and the heart was not displaced.

At operation on February 12, 1948, long segments of the four lowermost costal cartilages were resected, the xiphisternal joint and substernal ligament were cut through, the sternum freed from the intercostal structures, and a transverse cuneiform osteotomy was performed superiorly. The sternum was fractured into proper alignment and maintained by braided silk sutures placed through the bone. This corrected the deformity completely, leaving a space of about 6 cms. between the heart and the sternum which had pre-



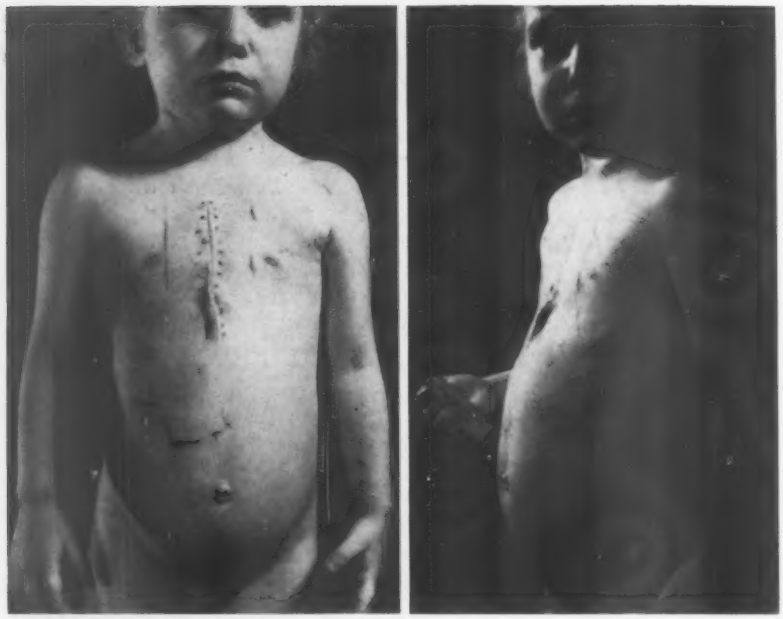
A B

FIG. 9.—Case 5. P. S., age 3 years. (A & B) AP and oblique views of child before operation.

viously been almost in contact. The soft tissues were repaired as in the previous instances. He was out of bed on the fourth day and was discharged on the seventh day with a satisfactory correction. The paradoxical respiration was abolished and the hollow was corrected, but a downward tilt from the angle of Louis (Fig. 8g) suggested that we might better have resected 5 costal cartilages on each side instead of 4.

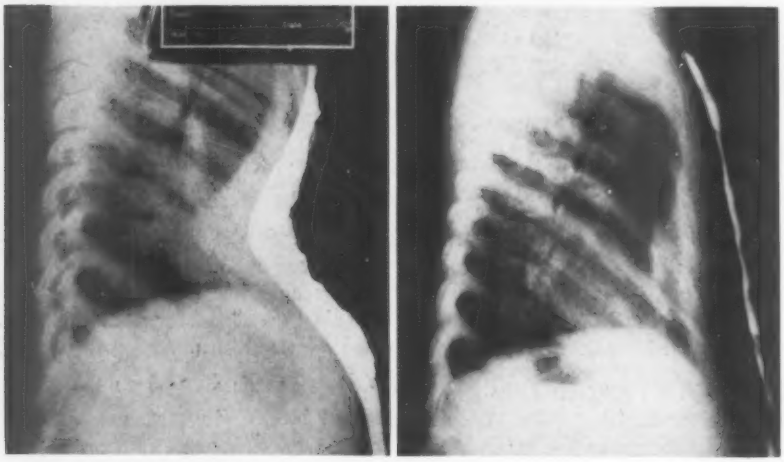
Case 5.—P. S., 457408. (Fig. 9) This 3-year-old girl had been known to have a "cavity in the front of her chest" from the time of birth. There were no other known instances of this deformity in the family. The child was first seen when she was two years old. The defect was marked. Operation was advised, but refused. A year later all observers were agreed that the defect was much more conspicuous, although asymptomatic. The excavation was a deep one, 6 cms. broad with maximal depth just above the xiphoid. The heart seemed to be displaced to the left. There was classical paradoxical inspiratory accentuation of the defect.

On April 13, 1948, all of the deformed portions of the lower 5 costal cartilages were removed, the xiphisternal articulation and subcostal ligament were cut through, the sternum



C D

FIG. 9.—(C & D) AP and oblique views of child taken a week after operation.



E F

FIG. 9.—(E) Preoperative roentgenogram. The barium outlines the hollow in the chest. The posterior surface of the sternum almost reaches the ventral surface of the vertebral bodies. (F) Postoperative roentgenogram. There has been a vast change.

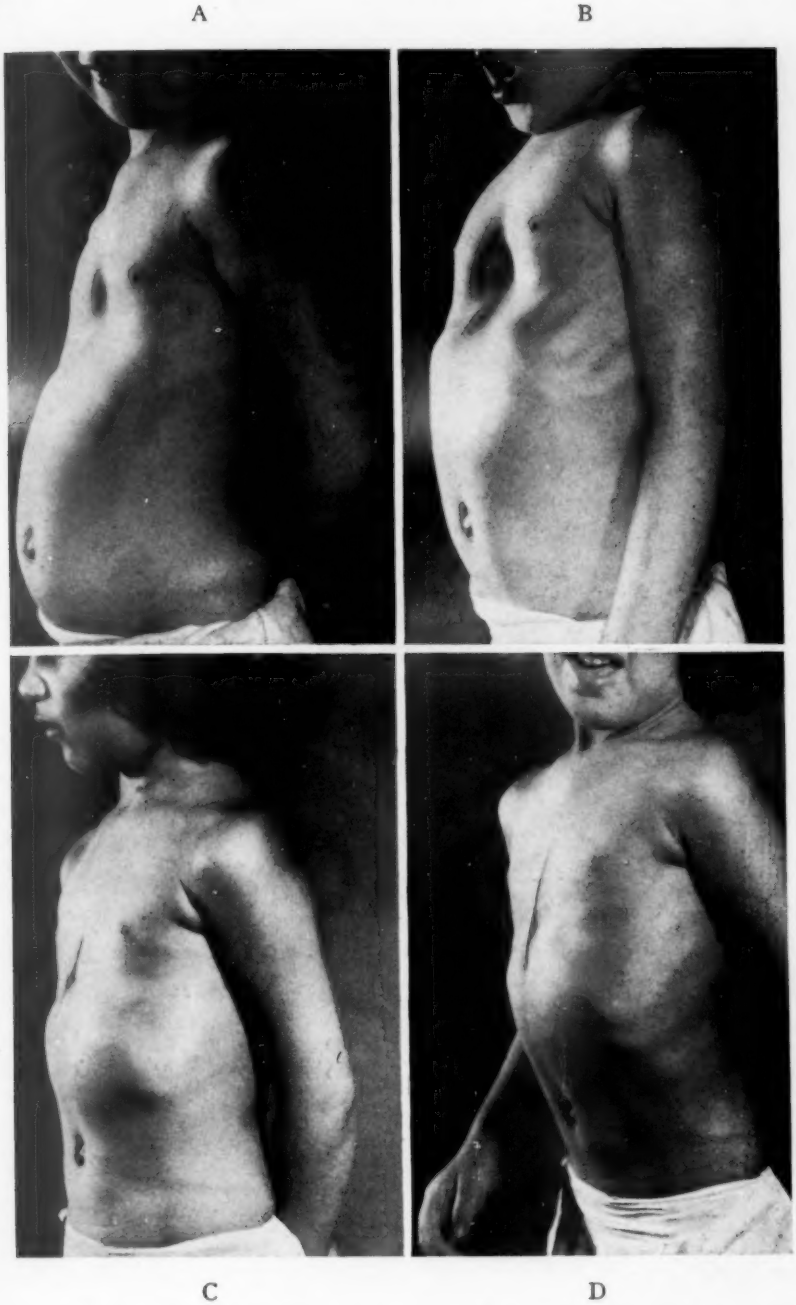
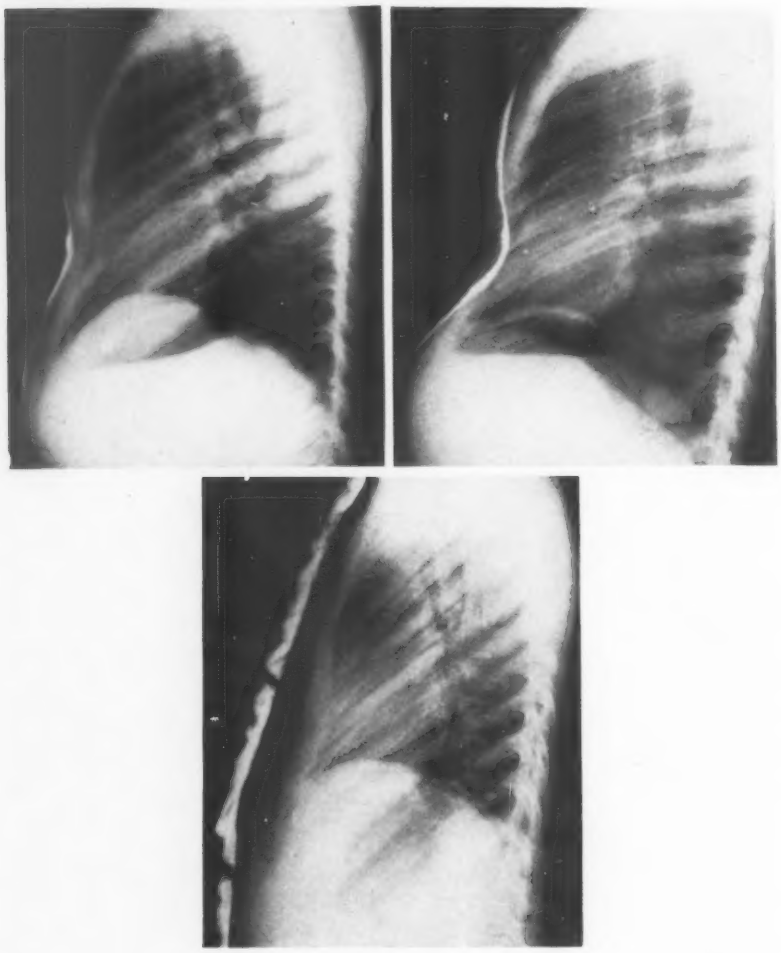


FIG. 10.—Case 6. B. P., age 5 years. (A & B) Before operation. Appearance at rest and on forced inspiration. Note paradoxical displacement of sternum on inspiration. (C & D) After operation. Appearance at rest and on forced inspiration. There is no paradoxical displacement of sternum and entire configuration of torso is much improved.

was freed, and a transverse osteotomy was performed just distal to the angle of Louis. A single suture of braided silk held the sternum in the corrected position. Bilateral pleural perforations were recognized during the operation and treated at its conclusion by pleural

E F



G

FIG. 10.—(E & F) Preoperative roentgenograms in expiration and inspiration. Paradoxical displacement of sternum is striking. (G) Postoperative roentgenogram. The barium stripe painted on the chest is deceptive. Close inspection shows that the sternum was fractured a little too low. Had five costal cartilages been removed on each side instead of three and the sternum then been fractured more cephalad, a more nearly perfect result would have been achieved.

aspiration. Except for a temperature of 100-101 degrees for the first 5 days, recovery was smooth and she left the hospital on the eleventh day with a good correction of her deformity by clinical and roentgenological examination.

Case 6.—B. P., 406240. (Fig. 10) This 5-year-old girl had been noted from birth to have a depression of her lower sternum. At the age of 7 months she had an adenoidectomy for wheezing respirations and at 12 months radium was applied to lymphoid tissue in the nasopharynx. Thereafter there was no respiratory difficulty. The parents were certain that the deformity had progressively increased in severity. On physical examination she showed typical pectus excavatum of moderate degree. The depression was not as deep, nor was as much of the sternum involved, as in the other patients. Paradoxical movement of the sternum with inspiration was fairly pronounced.

On June 3, 1948, operative correction was performed. Only 3 costal cartilages on each side were removed. The xiphoid was disarticulated, the sternum isolated, and a transverse osteotomy performed. The sternum was maintained in the corrected position with braided silk sutures. Convalescence was rapid and easy. She was up walking on the following day and left the hospital on the eighth day. The result, by physical and roentgenologic examination, was good.

Case 7.—R. S., 465631. This was a boy of 22 months whose chest deformity had been noticed since birth. The parents remarked that it had been increasing progressively, although he seemed to be well and had no symptoms. Physical examination showed an attractive child with a pronounced sternal concavity, both deep and broad. Paradoxical movement was conspicuous. In the roentgenogram the heart appeared slightly displaced to the left.

On June 29, 1948, operative correction was performed. The 4 lowermost costal cartilages on both sides were removed for the length of their deformity. The xiphisternal articulation was divided. A transverse sternal osteotomy was performed just distal to the angle of Louis and the sternum fractured anteriorly and maintained in this position by heavy silk sutures. The pleura was entered on the left. During the procedure it was obvious that the left edge of the sternum and the two or three lowermost costal cartilages on the left had pressed against the heart. The child convalesced smoothly and was discharged on the eighth postoperative day with a satisfactory correction.

Case 8.—C. L., 466265. This girl of 7 years had been born with a depressed sternum and her pediatrician referred her for operation because of increase in the degree of deformity. Her posture was poor and her exercise tolerance not equal to that of friends of the same age. Physical examination showed a child with a chest shallow in the anteroposterior diameter and with a conspicuous funnel deformity. The deformity was asymmetrical, being sharper and more acute on the right side than on the left. Paradoxical movement of the sternum was particularly prominent.

Operation was performed on August 3, 1948. Four costal cartilages were removed on each side, the sternum being treated in the usual fashion. She was out of bed and playing on the next day and left the hospital on the sixth day after operation. On the previous day 30 cc. of serosanguinous fluid was aspirated from the wound. The correction of the deformity was complete and in three weeks the chest wall felt solid.

SUMMARY

Pectus excavatum is a progressive deformity of the sternum and costal cartilages which may be satisfactorily corrected by operation. The younger the patient, the greater is the likelihood of attaining a completely normal thoracic contour. Operation is indicated for removal of a cosmetic defect which is a social handicap, for correction of a skeletal deformity, and for alleviation of cardiac or pulmonary symptoms. Early operation is important as a prophylaxis against progression of symptoms and signs.

The deformed portions of all the involved costal cartilages on both sides are resected. The xiphisternal articulation and the substernal ligament are divided and the body of the sternum isolated except for its attachment to the manubrium. A transverse osteotomy at the superior border of the defect permits the sternum to be elevated into the corrected position which is maintained by braided silk sutures in the bone. No external traction is employed and no type of cast or other support is required.

We have treated eight children ranging in age from 22 months to 10 years. In seven there were no complications and the results were excellent. One child died of a fulminating wound infection.

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THE TREATMENT OF ACUTE ANURIA*†

WITH EVALUATION OF PERITONEAL LAVAGE

IRVING A. FIELDS, M.D., HELEN EASTMAN MARTIN, M.D.,
D. G. SIMONSEN, PH.D., MAXINE WERTMAN, A.B.,
LEOLA WESTOVER, A.B.

LOS ANGELES, CALIF.

FROM THE DEPARTMENT OF SURGERY, COLLEGE OF MEDICAL EVANGELISTS, THE DEPARTMENT OF MEDICINE, SCHOOL OF MEDICINE, UNIVERSITY OF SOUTHERN CALIFORNIA AND THE LOS ANGELES COUNTY HOSPITAL

ACUTE ANURIA due to potentially reversible lesions, resulting from a variety of causes, *i.e.*, transfusion reaction, crush syndrome, sulfonamides, bichloride of mercury poisoning, shock, etc., but which are essentially similar in their histopathology, presents a therapeutic challenge to the clinician to prolong life until renal healing may occur.

Various procedures for possible alleviation of renal shutdown, such as intravenous procaine, spinal anesthesia or splanchnic block, or methods for reducing azotemia and prolonging life to the period of reversibility, such as peritoneal lavage[1, 2, 3, 4, 5, 6, 7, 8, 9] or the artificial kidney[10, 11] have been advocated in recent years. Several of the procedures are old[12, 13, 14, 15] but had not been adapted to clinical use until the work of Fine *et al.*[2, 3, 9]

This paper presents our experiences in the treatment of acute anuria in six patients with potentially reversible tubular lesions, and in one patient with acute glomerulonephritis. Four of our patients died and three lived.

DEFINITIONS

A 24-hour urinary output of 50 cc. or less was considered as anuria; between 50 and 100 cc. as oliguria.

METHODS

The technique of peritoneal lavage used in all but Case 1 (W. H.) was as follows: Under local anesthesia the inlet tube, a dePezzar catheter, was placed in the upper abdomen and the outlet tube, a Chaffin tube,[16] was guided into the pelvis by a uterine sound (Fig. 1). One of the limbs of the Chaffin tube was connected with an adequate length of rubber tubing and drainage accomplished by gravity, and the other limb was clamped off. Or, if mild continuous suction was applied to the first limb of the tube, the other limb was covered with sterile gauze and functioned as an air vent. The limbs were interchangeable. The wounds around each tube were closed snugly in layers with interrupted sutures, and the skin edges sealed with collodion-cotton.

Irrigating fluid was run in at the rate of approximately one liter every 45 minutes. The composition of the fluids we used compared with the solution used by Fine *et al*[2] is shown in Table I.

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† Preliminary report presented to the Los Angeles Surgical Society, March 14, 1947.

TABLE I.—*Composition of Lavage Fluids*

	*Modified Ringer's Lactate	*Modified Tyrode's	Modified Tyrode's (Fine et al.)
	Gm./liter	Gm./liter	Gm./liter
Sodium lactate	3.0	3.0	....
Sodium chloride	6.0	6.0	8.0
Potassium chloride	0.4	0.2	0.2
Calcium chloride	0.2	0.2	0.1
Magnesium chloride	....	0.1	0.1
Sodium acid phosphate	....	....	0.05
Sodium bicarbonate	....	....	1.0
Glucose	20.0	20.0	20.0
Added to each liter:			
Penicillin	20,000 units	20,000 units	2500–5000 units
Heparin	2–5 mg.	2–5 mg.	0.25–0.5 mg.

* Los Angeles County Hospital.

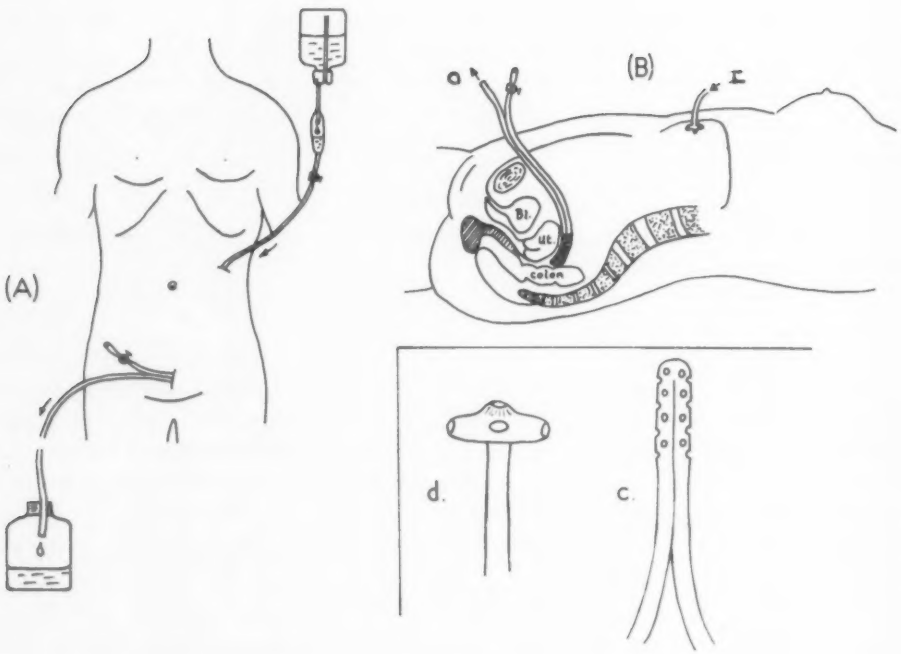


FIG. 1.—Diagram of peritoneal lavage. (A) Front view of abdomen with tubes in place. (B) Side view. I. Inlet—dePezzar catheter (d). O. Outlet—Chaffin tube (c).

The blood non-protein-nitrogen, chloride, carbon-dioxide combining power and sugar were determined daily. In addition, in several cases, a detailed electrolyte balance study was made on the serum and peritoneal-outflow-fluid, with daily determinations of the cations—sodium, potassium, calcium and magnesium—and the anions—chloride, bicarbonate and phosphorus. Blood pH, serum albumin and globulin and hematocrit levels were also determined. Serial electrocardiograms were taken on the majority of the patients. All chemical determinations were made by standard methods.

CASE SUMMARIES* WITH COMMENT ON THERAPY USED

Case 1.—W. H.—White male, age 32, (L. A. C. H. No. 974-738), was admitted to the hospital because of a suicidal attempt with tincture of iodine. There was a rapid development of methemoglobinemia, methemoglobinuria and acute anuria. Inadequate peritoneal lavage was performed from the 6th to the 9th hospital day, with retention of irrigating fluid due to plugging of the outflow tube. He received between 2000 and 3000 cc. of fluid intravenously daily during the first 5 days and later between 1000 and 2000 cc. daily. One-half to two-thirds of the total intravenous fluid contained sodium. Death occurred on the 9th hospital day.

Autopsy revealed acute pulmonary edema. There were a few strands of fibrin in the peritoneal cavity. The kidneys showed evidence of massive intravascular hemolysis, with one-half of the nephrons filled with hemoglobin casts. The microscopic diagnosis was obstructive and necrotizing lower nephron (tubular) nephrosis (Fig. 2-A).

COMMENT

This patient was overhydrated. He received too much intravenous fluid containing sodium. Also, absorption of irrigating fluid from the peritoneal cavity was facilitated by blockage of the outflow tube and the simultaneous intravenous administration of a hypertonic solution (10 per cent glucose).

Case 2.—R. O'N.—White male, age 21, (L. A. C. H. No. 1003-196), entered the hospital with a history of chills, fever, cough and chest pain of 10 days' duration which had been treated at home with an unknown amount of sulfathiazole and penicillin. On entry a diagnosis of pneumonia was made, and large amounts of penicillin were given. Despite this therapy he did poorly, developed a generalized edema, and progressive azotemia, with a good urinary volume. He received between 1500 and 2000 cc. of intravenous fluid daily. The urine was loaded with pus, bacteria (*E coli* and *gamma streptococcus*), and occasionally contained 15-20 red blood cells per high-power-field. A clinical diagnosis of sulfonamide nephrosis was made and peritoneal lavage was performed from the 16th to the 22nd hospital day, with clearance of 14-24 Gm. of non-protein-nitrogen per day. Death occurred on the 22nd hospital day.

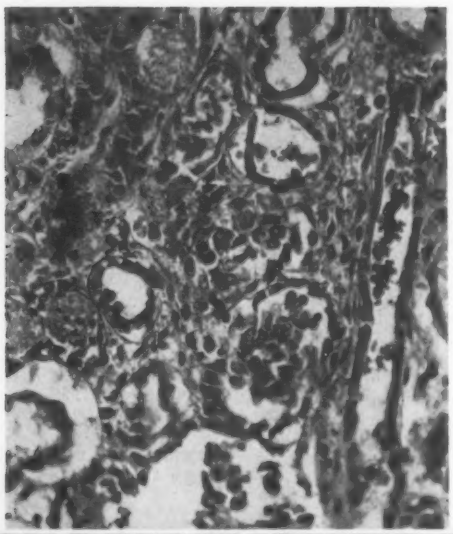
Autopsy revealed bilateral hydrothorax and pulmonary edema. There was an acute bacterial endocarditis. The renal lesion was an acute glomerulonephritis.

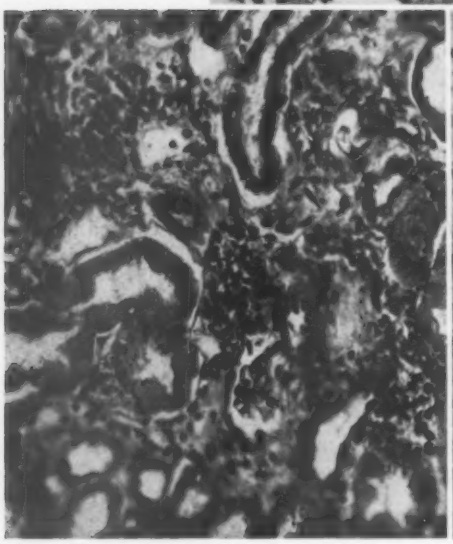
COMMENT

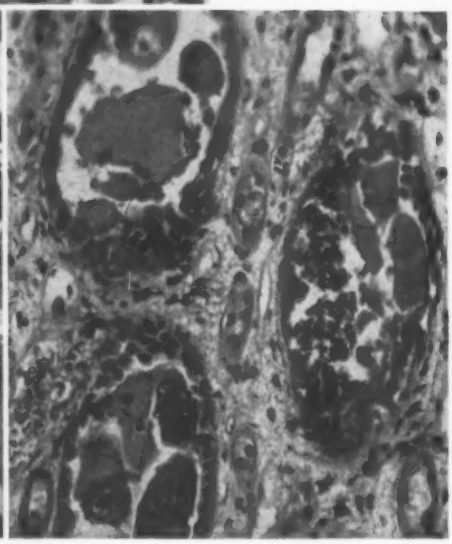
The correct diagnosis was not made in this patient. Since the majority of patients with acute glomerulonephritis survive the initial attack, it is questionable whether they should be candidates for peritoneal lavage. The lavage

* Drs. George Pearson, Raymond Bangle and Roy Byrnes assisted in the medical care and collection of laboratory material in several of the patients studied. Dr. Hugh Edmondson reviewed all the microscopic sections.

A







B C

FIG. 2.—Photomicrographs of kidneys. (A) (Case 1, W. H.—Iodine poisoning)—Obstructing and necrotizing lower nephron (tubular) nephrosis. (B) (Case 3, H. N.—Transfusion reaction)—Healing lower nephron nephrosis. (C) (Case 4, M. G.—Bichloride poisoning)—Necrotizing upper nephron nephrosis with moderate regeneration and internal hydronephrosis. (See text for details.)

worked well in clearing nitrogenous waste products, but the patient died of pulmonary edema. This patient likewise received too much intravenous fluid.

Case 3.—H. N.—White woman, age 66, (L. A. C. H. No. 1002–896), entered the hospital for a resection of a carcinoma of the rectum. She had a transfusion reaction on the 22nd hospital day while being prepared for surgery. Oliguria and progressive azotemia developed. Peritoneal lavage was started 6 days after the transfusion reaction, and was continued for 11 days with marked improvement in the azotemia. She received between 1000 and 1500 cc. of intravenous fluid daily. Five days after the lavage was started generalized edema developed. This persisted and the patient died of pulmonary edema 19 days after the transfusion reaction. The 24-hour urine volume had reached normal levels 2 days before death.

Autopsy revealed severe pulmonary edema, an early bronchopneumonia, interstitial myocarditis, and a grade 3 squamous cell carcinoma of the rectum. The kidneys showed a healing lower nephron nephrosis with severe interstitial pyelonephritis (Fig. 2-B).

COMMENT

This patient began putting out urine before her death, and it is noteworthy that the microscopic sections of her kidneys showed advanced healing of the tubular lesion. The use of a retention catheter was probably the cause of the ascending pyelonephritis. She received entirely too much intravenous fluid, a good share of which was hypertonic, and her circulation was overloaded. It is probable that cardiac failure due to the interstitial myocarditis was also a contributing factor in her edema and death.

Case 4.—M. G.—White woman, age 32, (L. A. C. H. No. 1009–649) entered the hospital because of ingestion of bichloride of mercury in a suicidal attempt. BAL was started within 6 hours of taking the bichloride of mercury and a full therapeutic course was given. Severe oliguria developed early and persisted for 21 days until her death. Peritoneal lavage was started on the 6th hospital day and was used continuously for 9 days. It was stopped for several days because of the development of peritonitis, but with the subsidence of peritoneal irritation, intermittent lavage was re-instituted later. There was effective clearing of nitrogenous waste products by this procedure. Intravenous fluids (isotonic) were restricted to 1000 cc. per day except during the last few days of life when she received additional concentrated plasma and concentrated human albumin. She died on the 22nd hospital day of pulmonary edéma.

Autopsy showed bilateral hydrothorax (minimal) and marked pulmonary edema. The kidneys showed a necrotizing upper nephron nephrosis, with moderate regeneration, and a marked internal hydronephrosis secondary to blockage of the collecting tubules by great numbers of casts, some of which were replicas of dead epithelium from the upper nephron (Fig. 2-C).

COMMENT

This patient received too much intravenous fluid, especially in the last seven days of her life. It is doubtful if she ever could have put out urine through the blocked collecting tubules, but the immediate cause of her death, as in the others, was acute pulmonary edema. In addition to the intravenous fluid, she undoubtedly absorbed fluid from the peritoneum, especially during the time she received concentrated plasma, and concentrated human albumin intravenously.

Case 5.—B. B.—Negro female, age 30, (L. A. C. H. No. 974–738). Prior to entry to the hospital, this woman had a septic abortion and was anuric at the time of hospitalization. (The exact cause of the renal suppression was never established.) She received between 2000 to 3000 cc. of intravenous fluid daily during the first 5 days (of which 1000 cc. was normal saline) and developed generalized edema. Restriction of fluid and sodium was begun on the 6th hospital day, and peritoneal lavage was performed from the 6th to the 10th day with good clearance of nitrogenous waste products. On the 9th hospital day, her urinary output was 460 cc. with gradual increase in volume thereafter. The specific gravity of the urine remained at 1.010 for 82 days.

COMMENT

This patient began putting out urine on the 9th hospital day. She probably would have gotten well without peritoneal lavage. Her spontaneous recovery thus was not jeopardized by overtreatment.

Case 6.—"X"—White woman, age 32 (outside hospital). This patient had a Porro Cesarean section and a day later was re-operated on for an actively bleeding cervical stump vessel. She was transfused several times and was believed to have had a transfusion reaction. Following this, she became severely oliguric and developed progressive azotemia. She received on successive days: 3800, 1700, 1250, 500, 1000, 700, 1150 cc. of intravenous fluid. On the 8th hospital day she developed marked generalized edema and a pericardial friction rub. Peritoneal lavage was performed for 24 hours starting on the 9th hospital day. Intravenous fluids were discontinued immediately preceding the institution of lavage and the oral intake limited to an occasional sip of tap water. During the next 3 days generalized muscular twitchings developed. She showed definite improvement on the 12th hospital day and was able to take a modified soft diet. The 24-hour urine volume was normal by the 14th day, but the specific gravity remained at 1.010 for nearly 3 weeks.

COMMENT

It is quite likely that this patient would have improved without peritoneal lavage since this was continued for only one day. It did bring the blood non-protein-nitrogen down temporarily, and clinically she appeared more alert following its use. She had a moderately severe generalized edema which disappeared rapidly with the restriction of fluids and sodium. The elimination of intravenous fluids and sodium ions probably saved this patient from overhydration and death from pulmonary edema.

Case 7.—W. O'Q.—White male, age 37, (L. A. C. H. No. 1004–828) attempted suicide with bichloride of mercury. BAL was started within 2½ hours of the bichloride ingestion. The patient became anuric within 6 hours. After the 5th hospital day intravenous fluids were discontinued and oral fluids were restricted to 500 to 800 cc. daily. Gastric lavage was performed for 2 days with clearance of approximately 3.3 Gm. of non-protein-nitrogen per day. The 24-hour urine volume reached a normal level by the 9th hospital day. The specific gravity remained low for 6 weeks.

COMMENT

The only intravenous fluid administered to this patient after the 3rd hospital day was procaine: 1 Gm. in 250 cc. of 2½ per cent glucose in water, repeated 3 times at 12-hour intervals. He is the only patient in our series who never developed any edema. In spite of a strictly limited oral fluid intake (500–800 cc. per day) he had a diuresis after the 9th day. He probably would

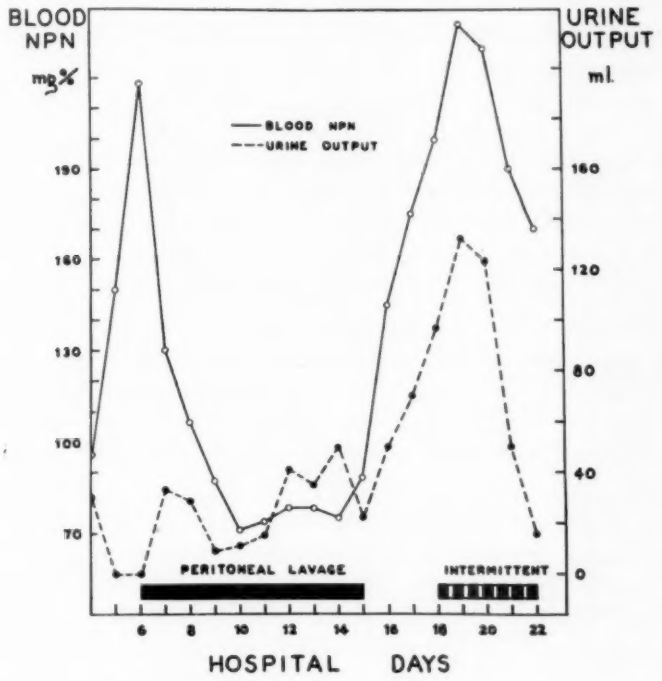


FIG. 3.—(Case 4, M. G.—Bichloride poisoning) Results of peritoneal lavage on blood non-protein-nitrogen level.

TABLE II.—*Adequate Urine Volume in Lower Nephron Nephrosis**

Hospital Day	Urine Volume in cc. (1)	Blood NPN mg. %	Blood Sugar mg. %	CO_2 C.P. Vols. %	Comment
1	over 1300	75	1300	13	Shock
2	over 1700	59	362	26	Cold right leg
3	over 2300	45	..	..	
4	over 1300	..			Sulfadiazine started
5	over 600	..	..	..	for *E. coli* sepsis
6	over 1000	..	..	..	
7	over 1000	..	..	..	
8	over 1000	..	148	57	
9	1300	..	..	..	
10	over 1100	..	..	..	
11	over 2200	174	..	..	
12	3000	..	..	..	
13	825	175	..	..	
14	1200	176	..	..	
15	1400	..	..	..	
16	2100	205	185	40	
17	1750	..	..	..	
18	1250	215	..	..	
19	....	..	..	..	Death

* History not discussed in paper as patient treated prior to present series. 56-year-old Negro male, entered in severe diabetic acidosis and shock. *E. coli* sepsis. Circulatory failure and gangrene of right leg (packed in ice). Autopsy showed lower nephron nephrosis due to shock and sulfonamides.

(1) Some of urine discarded without measuring; the amount recorded actually measured.

have recovered even if nothing (except BAL) had been done for him, but at least his recovery was not complicated by injudicious overhydration and sodium ion administration.

DISCUSSION

Many case reports have demonstrated that peritoneal lavage[1, 2, 3, 4, 5, 6, 7, 8, 9] is an effective means of removing nitrogenous waste products. The results in the six of our patients who had peritoneal lavage confirm this and are illustrated in Fig. 3 (Case 4—M. G.) which shows a drop in the blood non-protein-nitrogen from 218 to 71 mg. per cent with 4 days of peritoneal lavage (hospital days 6 through 9).

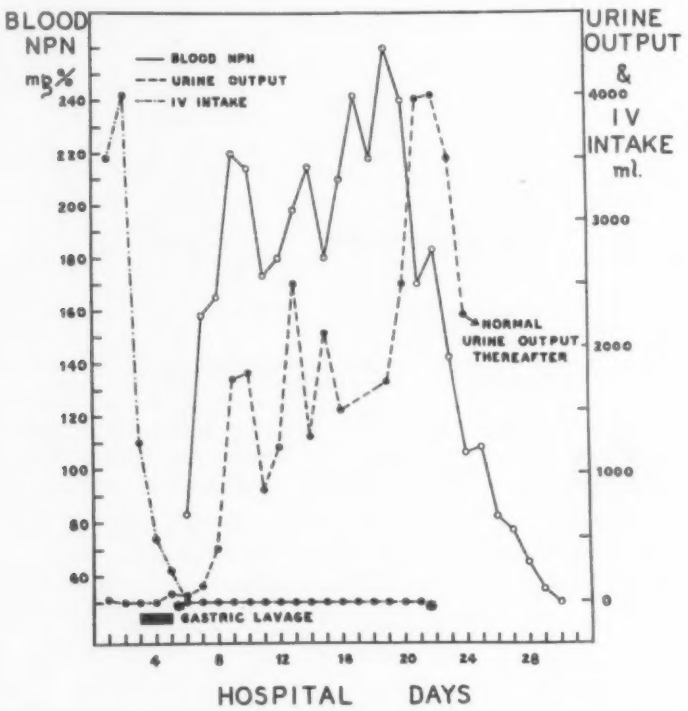


FIG. 4.—(Case 7, W. O'Q.—Bichloride poisoning) Intake, output and blood non-protein-nitrogen level.
* No intravenous fluids between hospital day 5 and 21; oral intake under 800 cc. per 24 hours.

The characteristic microscopic pathology found in these acute lesions of either the upper or lower nephron are well illustrated in Fig. 2 and require no comment due to the thorough description of Mallory[17] and others.[18] Certain points, however, have previously received little or insufficient emphasis. Some patients with acute tubular lesions may have no anuria or oliguria. In spite of tubular damage they may have an adequate 24 hour urine volume. This urine has a low specific gravity and presumably comes from only a few functioning nephrons. Progressive azotemia does develop, however, just as when

anuria or oliguria is present. This is illustrated in Table II (lower nephron nephrosis due to shock and sulfonamide injury) which shows a 24 hour urine volume usually over 1 liter, with a blood non-protein-nitrogen which steadily rose from 45 to 215 mg. per cent before death. Other patients may have several days of oliguria, and then put out an adequate 24 hour urine volume, but the blood non-protein-nitrogen level continues to rise since only a few nephrons are functioning. Fig. 4 (Case 7—W. O'Q., upper nephron nephrosis due to bichloride of mercury poisoning) shows a blood non-protein-nitrogen which rose from 158 to 260 mg. per cent, with 24 hour urine volumes between 800 and 3800 cc. from the 8th day to the 20th day. The fact that spontaneous diuresis will occur even with marked restriction of fluids is also seen in Figure 4. This patient had marked restriction of fluid intake after the 3rd day of anuria, but had a spontaneous increase in the 24 hour urine volumes from 125 cc. to 1750 cc. between the 7th and 9th days.

The problem of fluid and sodium retention has not been stressed sufficiently except by a few.[19, 20, 21, 22] All of the patients in our series (except one, Case 7) were edematous at the time we were first consulted about their anuria. The importance of this problem is seen in the fact that the immediate cause of death in the four patients who died was severe pulmonary edema. The only patient who did not develop edema at any stage received only a small volume of intravenous fluid on the 3rd and 4th hospital days, and none from the 5th to the 21st hospital day (Figure 4).

It is obvious that with loss of the excretory function of the kidneys, in particular tubular function, the main control of extracellular sodium is lost. If any sodium is given it will be retained,[23] and will hold water with it. Barring severe loss of intestinal fluids (continuous nasogastric suction, diarrhea, etc.) there should be little loss of extracellular sodium and consequently little if any replenishment should be required. If acidosis of severe degree develops administration of a small amount of sodium may be necessary. This is preferably given orally in small doses (4.0 Gm. of sodium bicarbonate) and repeated until the acidosis is moderately improved.

There is no evidence that alkalinization following a transfusion reaction or sulfonamide injury reverses the damage already done. Forcing fluids in anuria does not raise the glomerular filtration pressure or break "the tubular block," but merely increases the circulating blood volume[24] due presumably to diffusion of the glomerular filtrate into the peritubular capillaries.

Another reason for rigid restriction of intravenous fluids and sodium is based on the fact that patients late in the course of anuria tend to develop pulmonary edema spontaneously. This is presumed to be due to some ill-defined toxic effect of retention products on the alveolar capillaries.

With the onset of diuresis, in the recovery phase, the management as to fluids and electrolytes may vary from the above plan. Rapid and perhaps fatal loss of electrolytes may occur at this time. Sodium loss if present and indicated by acidosis or measurement of blood and urine sodium levels should be corrected by adequate replacement.

TABLE III.—*M. G. No. 1009–649 Case 4*

	DAY 4		DAY 5		DAY 6		DAY 7		DAY 8		DAY 9		DAY 10		DAY 11		DAY 12		DAY 13	
	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid
Cations																				
Na mEq.	127	...	122	...	132	113	...	130	...	123	144	132	142	132	149	129	143	130	159	137
K mEq.	3.2	...	3.4	...	3.7	3.6	4.0	3.1	3.9	2.8	3.7	2.8	3.6	3.2	3.9	2.9	3.6	2.9	3.6	4.0
Ca mEq.	4.4	...	4.4	...	4.3	3.1	4.8	3.3	5.4	3.5	5.2	3.8	5.8	3.8	5.8	3.7	5.9	3.8	5.8	3.8
Mg mEq.	2.4	...	2.6	...	2.5	0.7	1.7	1.0	1.8	1.3	1.8	1.3	1.9	1.2	1.7	1.3	2.2	1.4	2.1	0.9
Anions																				
HCO_3 mEq.	14	...	7	...	14	...	9	...	16	...	18	...	23	...	19	...	24	...	27	...
C1* mEq.	72	...	72	...	76	96	57	91	70	82	79	103	77	85	77	90	83	107	84	102
HPO_4 mEq.	4.0	...	5.7	...	5.2	1.4	3.2	1.3	2.6	0.8	2.6	0.6	2.2	0.8	3.1	1.0	2.7	1.0	2.3	0.8
pH	7.40	...	7.41	...	7.24	...	7.38	...	...	...	7.50	...	7.48	...	7.50	...	7.58	...	7.56	...
Hematocrit %	...	...	33	...	31	...	31	...	...	...	30	...	31	...	29	...	25	...	22	...
NPN* mg. %	93	...	150	...	218	110	130	105	107	75	87	50	71	50	73	59	78	43	78	40
Creatinine* mg. %	6.8	...	8.4	...	10.0	7.0	7.2	...	6.0	6.3	7.1	6.0	6.0	6.1	5.5	4.0	4.8	4.1	3.2	3.2
Albumin Gm. %	4.0	...	4.3	...	3.6	...	4.0	...	4.1	...	4.0	...	4.1	...	3.8	...	4.1	...	3.9	...
Globulin Gm. %	2.3	...	2.6	...	2.0	...	2.1	...	2.3	...	2.4	...	2.7	...	2.6	...	2.9	...	3.0	...
Total Protein Gm. %	6.3	...	6.9	...	5.6	...	6.1	...	6.4	...	6.4	...	6.8	...	6.4	...	7.0	...	6.9	...
Sugar* mg. %	123	...	117	...	190	1000	173	820	198	710	203	784	214	708	190	1152	178	1314	147	1070

*Whole blood.

	DAY 14		DAY 15		DAY 16		DAY 17		DAY 18		DAY 19		DAY 20		DAY 21		DAY 22		DAY 22a.	
	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit. Fluid	Serum	Perit† Fluid
Cations																				
Na mEq.	142	132	142	130	144	...	146	...	142	129	139	121	139	130	...	134	...	130	139	...
K mEq.	4.5	4.3	5.4	4.1	6.6	...	7.0	...	7.4	4.4	6.4	2.6	7.1	3.6	6.3	3.9	...	3.3	...	...
Ca mEq.	5.5	3.7	5.3	3.6	5.0	...	4.9	...	4.5	3.6	4.4	4.0	4.2	3.8	4.4	3.4	4.6	3.6	4.6	...
Mg mEq.	1.8	0.7	1.7	1.2	2.0	...	2.3	...	2.5	1.4	2.3	1.3	2.2	1.4	2.1	1.3	2.1	1.1	2.4	...
Anions																				
HCO_3 mEq.	25	...	22	...	23	...	22	...	18	...	18	...	19	...	20	...	...	...	...	...
C1* mEq.	71	99	79	107	70	...	70	...	68	48	82	109	81	97	79	102	79	100	83	...
HPO_4 mEq.	2.2	0.8	2.3	1.2	3.2	...	3.8	...	4.9	1.9	5.1	0.0	4.2	0.7	3.1	1.0	2.5	0.6	3.4	...
pH	7.56	...	...	...	7.50	...	...	...	7.46	...	...	...	...	...	...	...	...	...	...	...
Hematocrit %	27	...	...	...	31	...	31	...	29	...	28	...	25	...	24	...	...	...	...	...
NPN* mg. %	75	56	88	59	145	...	175	...	200	131	238	11	230	30	190	135	170	70	150	...
Creatinine* mg. %	4.1	4.2	4.9	5.9	9.0	...	9.5	...	13.0	7.9	10.3	1.2	8.9	5.5	7.3	6.7	...	3.8	5.5	...
Albumin Gm. %	3.4	...	3.2	...	3.4	...	3.5	...	3.7	...	3.4	...	3.3	...	3.0	...	3.1	...	3.2	...
Globulin Gm. %	2.8	...	2.8	...	3.0	...	2.9	...	3.0	...	2.7	...	2.5	...	2.2	...	2.4	...	2.5	...
Total Protein Gm. %	6.2	...	6.0	...	6.4	...	6.4	...	6.7	...	6.1	...	5.8	...	5.2	...	5.5	...	5.7	...
Sugar* mg. %	128	885	155	816	103	...	110	...	134	1372	268	1700	138	1500	178	...	138	1860	193	...

* Whole blood. † Eight-hour period.

The treatment of shock and anuria when they co-exist is a more difficult problem. Initially, dehydration and shock and their underlying causes are to be treated vigorously with sodium-containing fluids, whole blood, or plasma, and every attempt made to rapidly restore and maintain normal circulating blood volume and electrolyte levels. It takes usually 24 or more hours to establish the existence of anuria in a given patient and during that interval, treatment of shock or dehydration and sodium and fluid loss should be prompt and vigorous. If the circulating blood volume and electrolyte levels have been adequately restored but the patient after 24 to 48 hours still remains in shock *and* anuria, the forcing of intravenous fluids and sodium from this point on is not only ineffective but may, on the contrary, result in overloading of the circulation and fatal pulmonary edema.

Since no one to date has found a satisfactory substance to add to the peritoneal lavage fluid to exert an osmotic effect comparable to that of plasma proteins, appreciable amounts of fluid may be absorbed from the peritoneal cavity with long continuous lavage. This is well demonstrated in Case 4 (M. G.—Table 3—upper nephron nephrosis due to bichloride of mercury) who was lavaged continuously for 9 days and intermittently for 4½ days with a steady decline in the level of the serum albumin from 4.0 to 3.2 Gm. and hematocrit from 33 per cent to 22 per cent. The absorption of fluid from the peritoneal lavage is accelerated if hypertonic intravenous fluids are administered simultaneously.[13]

Hypertonic fluids, such as concentrated salt-poor human albumin and hypertonic glucose, are contraindicated at all times even if lavage is not being performed due to the fact that they rapidly increase the circulating plasma volume and may precipitate acute pulmonary edema.

The problem of the total electrolyte balance has received little emphasis in the treatment of acute anuria. Our studies suggest that important alterations in the electrolytes occur, some of which can be corrected. Many different types of change may occur early in the course of anuria due to loss of fluid and electrolytes in diarrheal fluid, vomitus, hemorrhage, etc. Late in the course of anuria electrolyte changes due to tissue breakdown may occur. These electrolyte changes are illustrated in Table III, Case 4 (M. G.—bichloride of mercury poisoning). Early in the anuria (5th day) the serum levels of sodium, potassium, calcium and chloride were low, probably due to loss by diarrhea and vomiting which were present. The serum magnesium was high early; the mechanism of this is not clear. It was possible to restore these electrolytes to almost a normal level with peritoneal lavage. The composition of the lavage fluid was varied therefore as the electrolytes, particularly potassium, changed. Figure 5 (Case 4—M. G.—bichloride of mercury poisoning) shows the clearance or retention of electrolytes by peritoneal lavage fluid as compared with the serum electrolyte levels in the same patient. After initial adjustment of the serum deficits or excesses present it is noted that the serum sodium and calcium remained relatively constant. Chloride was absorbed from the lavage fluid throughout indicating a chloride depletion (this patient had nasogastric

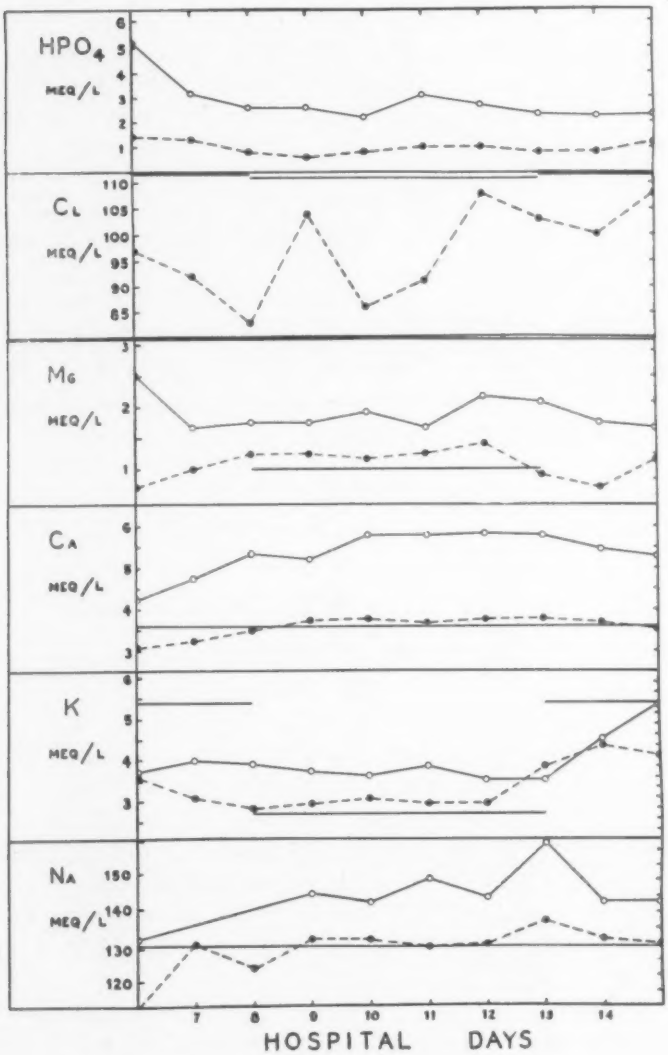


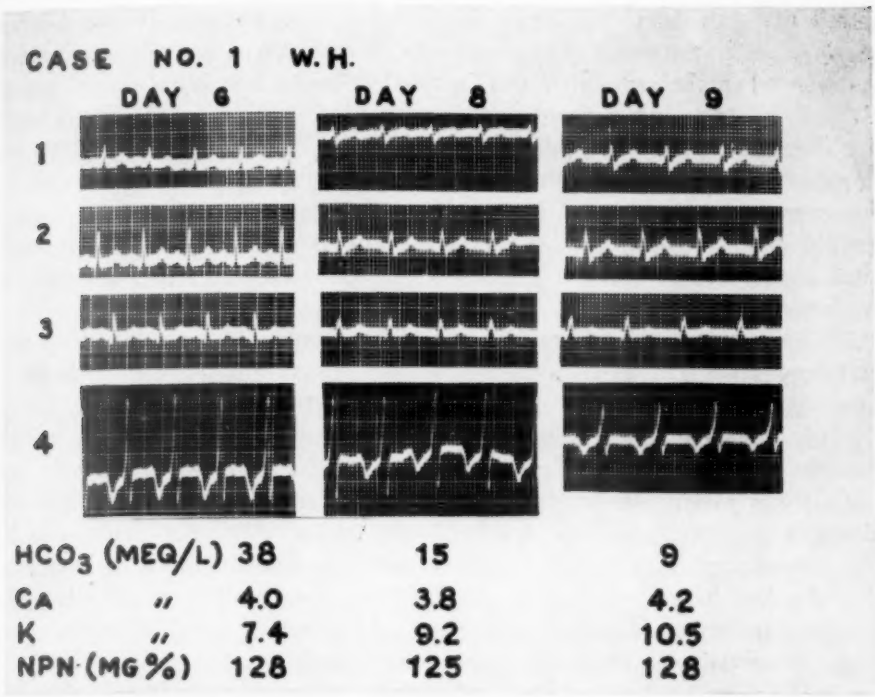
FIG. 5.—(Case 4, M. G.—Bichloride Poisoning) Clearance or retention of serum electrolytes by peritoneal lavage.

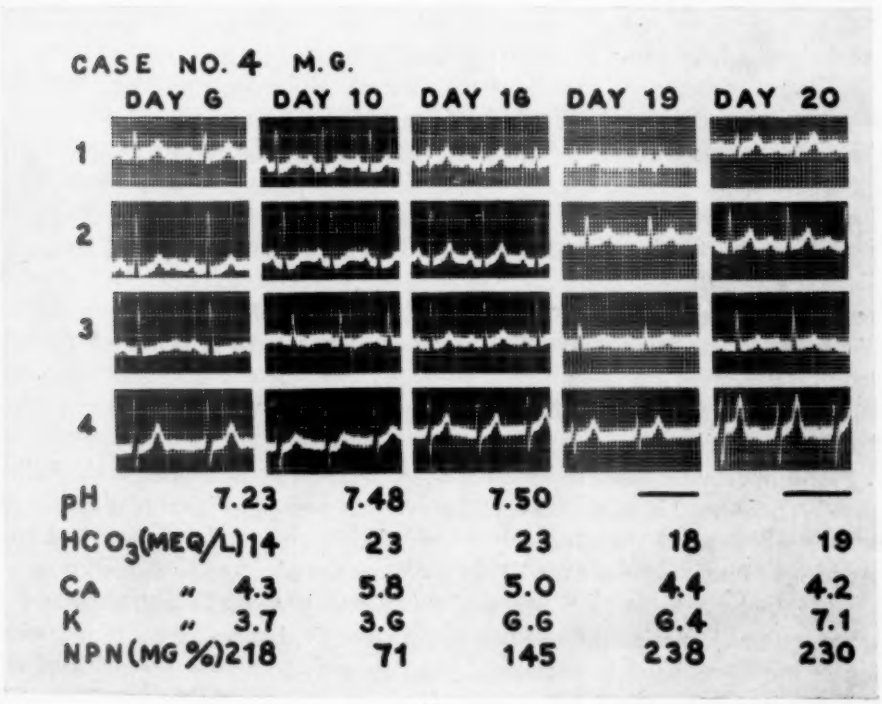
The solid line indicates the concentration in the peritoneal inflow fluid. A change in the position of the line coincides with a change in composition of the inflow fluid.

The dotted line with the solid circles represents the concentration in the peritoneal outflow fluid. The line with the open circles indicates the serum concentration.

The serum concentration of chloride is not given as the determinations were made on whole blood.

A





B

FIG. 6.—Correlation of the electrolyte changes with the electrocardiogram.

suction at intervals). Potassium was retained throughout most of the course (until the 13th day)—the serum levels being low. Ringer's-lactate solution was used when the serum potassium was definitely low, and modified Tyrode's solution when the potassium was in the low normal or high normal range. Actually a lavage fluid without potassium should be used when the serum levels are definitely elevated. A drop in the serum potassium occurred with the development of peritonitis; the mechanism of this is not clear. Terminally, the serum potassium levels rose, presumably due to tissue breakdown. The pH of the blood which is known to affect the ratio between serum and cellular potassium concentrations did not appear to be a primary factor in the variations encountered here.

These results demonstrate that the electrolytes vary from period to period and consequently the electrolyte level should be carefully followed in order to properly treat the patient.

If chemical determinations of the electrolytes cannot be made, certain changes in acid-base equilibrium, serum potassium and calcium levels and occasionally magnesium levels may be gauged from their known effects on the electrocardiogram, if serial tracings are taken.[25, 26, 27, 28, 29, 30, 31] If the T-waves change from normal amplitude to a very low amplitude, it is suggestive of a drop in serum potassium, or, if from normal to high amplitude, a rise in serum potassium is to be suspected. Development of conduction blocks, or of an idioventricular rhythm suggests a very high serum potassium level. A long QT-interval (period of electrical systole) suggests hypocalcemia, although this may also be due to a low serum potassium. Differentiation can usually be made by the height and character of the T-waves.

Electrolyte changes correlated with the electrocardiogram and illustrating these points are shown in Fig. 6-A (Case 1—W. H.) and Fig. 6-B (Case 4—M. G.) The effect of a very high serum potassium (10.5 mEq.) on the electrocardiogram is seen in A (Case 1—W. H.—on the 9th day), where there is a loss of the P-waves, and an intraventricular block of the right bundle branch type. The effect of low potassium (3.6 mEq) is seen in Fig. 6-B (Case 4—M. G.) on the 10th day. Here the T-waves are low in amplitude. As the serum potassium increased from 6.6 mEq. to 7.1 mEq. from the 16th to 20th day, the T-waves became more elevated. The effect of low serum calcium on the QT-interval is seen in Fig. 6-A (Case 1—W. H.) on the 8th day when the serum calcium was 3.8 mEq. and the QT-interval 0.34 seconds, compared to a calculated normal of 0.29 seconds.

An important consideration in the treatment of acute anuria is the indication for peritoneal lavage. It is well known that patients with reversible tubular lesions will recover spontaneously provided they are not fatally overhydrated. At present our indications for lavage have narrowed down to the following:

(1) Hyperpotassemia. Deficits of this electrolyte can be corrected by oral or parenteral administration of potassium chloride, but an excess of potassium ion in the blood must be brought down promptly to a near normal level and this can be accomplished by the use of a proper lavage fluid. *(2) Electrolyte Imbalance.* Multiple deviations from the normal electrolyte pattern frequently

can be corrected by the use of a proper lavage fluid. *(3) Severe Azotemia*—when it is accompanied by toxic symptoms such as restlessness, disorientation, diplopia, convulsions, generalized twitchings, etc. Any two or all of the above indications may overlap.

Six of our patients received peritoneal lavage. In the first patient (Case 1—W. H.—iodine poisoning) it was a failure due to technical difficulties and fluid retention. Case 5 (B. B.—septic abortion) would have recovered without peritoneal lavage, as would have Case 6 ("X"—transfusion reaction). It did aid in the latter two cases in clearing edema and Case 6 seemed clinically improved, but this is obviously difficult to evaluate. Case 2 (R. O'N) had an acute glomerulonephritis and probably should not have been lavaged. The role of lavage in Case 3 (H. N.—transfusion reaction) and Case 4 (M. G.—bichloride of mercury poisoning) who received prolonged peritoneal lavage (over ten days) is difficult to evaluate. Both of these patients had good chemical results from the lavage, but died of pulmonary edema, due to too much intravenous fluid.

One advantage of peritoneal lavage is the nutritional one, since glucose is readily absorbed from the peritoneum. This may be important in a patient unable to retain food by mouth, and in whom intravenous fluids must be restricted.

It should be emphasized that peritoneal lavage is not a simple procedure, and if used without expert supervision it may actually contribute to a fatal outcome. All of our patients in whom peritoneal lavage was used for more than a short interval (Cases 1, 2, 3 and 4) developed bacterial contamination of the peritoneum despite the use of penicillin (100,000 units intramuscularly q.3 h.) In all the autopsied patients the peritonitis was localized and healing was not considered to be a factor in death. A detailed discussion of various factors in the pathogenesis of the peritonitis is beyond the scope of this report. Strict and continued aseptic technique and avoidance of hypertonic irritating solutions over a prolonged time will minimize but not entirely prevent peritonitis.

ROLE ØF VASOSPASM

The role of vasospasm in the production of anuria has been re-emphasized in the work of Truetta.[32] Various agents to counteract this vasospasm, such as intravenous alcohol, procaine,[33] spinal anesthesia and splanchnic block,[34] have been suggested. We have tried all of these agents. It has been difficult, however, to critically evaluate the results in our patients since other therapeutic agents have been used simultaneously except in Case 7 (W. O'Q—upper nephron nephrosis) who received intravenous procaine (3 Gm.) on the 3rd and 4th day of his anuria, without any effect on the urine output (Fig. 4). Further critical evaluation of agents to counteract vasospasm should be made.

TREATMENT

As soon as a situation arises, such as dehydration, shock, transfusion reaction, etc., which may precipitate acute anuria, every effort is made to correct

the blood volume and serum sodium level. After anuria occurs, all intravenous fluids and sodium are eliminated, with the possible exception of procaine and citrated blood transfusions. If the patient is able to take fluid and food by mouth the oral intake is limited to 500–800 cc. of water per day, and a low salt diet, less than 1 Gm. per day, is used. The sodium ion is administered only to correct severe acidosis. If the carbon dioxide combining power drops to or below 25 volumes per cent the patient is given small doses of sodium bicarbonate (4 Gm.) by mouth with repeated checks of the carbon dioxide combining power.

In these patients with anuria it is well to remember that selective reabsorption and automaticity of maintenance of electrolyte pattern are lacking and that small doses of ions may produce a far greater effect on blood chemistry than would ordinarily occur if renal function were normal.

If the patient is seen in the first 48 hours after anuria develops intravenous procaine is used: 1 Gm. in 250 cc. of 2½ per cent glucose in water, given over a period of 20 minutes and repeated every 12 hours for 2 to 3 doses.

Penicillin is used routinely (whenever lavage is instituted). Streptomycin and blood transfusions are used as indicated. (In the presence of anuria streptomycin blood level is built up rapidly and should be used with caution). We do not attempt to maintain an adequate protein intake during the critical period of anuria, as this interval is short (10 to 14 days). The restoration of weight and normal nutritional status occurs rapidly after the return of kidney function and has presented no problem. Vitamins C and B_1 are given parenterally.

Daily determination of CO_2 blood chlorides, non-protein-nitrogen, sodium and potassium are made. Close and frequent observations are made for evidence of peripheral pitting edema or signs of pulmonary edema. The decision to institute peritoneal lavage (or gastric lavage) is based on criteria discussed above. The treatment of pulmonary edema, once established, is difficult but venesection with rapid removal of 500 cc. of blood has often produced dramatic (although temporary) improvement. Oxygen inhalation under pressure breathing has also been helpful.

During the recovery diuresis phase the fluid and sodium chloride intake are increased to compensate for the increased loss in the urine. It should be re-emphasized that this phase may be a critical one: The urine has a low specific gravity and resembles the glomerular filtrate; the 24 hour urine output may reach 2500 to 4000 cc. and large quantities of electrolytes may be lost daily in that volume.

SUMMARY

Six patients with anuria due to potentially reversible tubular lesions were treated with peritoneal or gastric lavage. Three of these patients died and three lived. In addition, one patient who died of an acute diffuse glomerulonephritis was treated with peritoneal lavage. Those who lived would have probably survived without peritoneal or gastric lavage.

Peritoneal lavage was: (1) effective in removing substantial amounts of

nitrogenous waste products; (2) helpful in adjusting a disturbed electrolyte pattern, especially potassium; (3) an indirect means for supplying glucose. The disadvantages of peritoneal lavage were: (1) a technical procedure which required constant and expert supervision and special nursing; (2) peritoneal contamination (appearance of bacterial organisms in the outflow fluid) in nearly all cases in which lavage was continued for more than four days; (3) absorption of fluid from the peritoneal cavity occurred if hypertonic intravenous fluids were administered simultaneously.

Gastric lavage, used as the primary lavage method in one case, was much less effective in comparison with peritoneal lavage. On the other hand, it did not have the latter's disadvantages.

Acute pulmonary edema was the immediate cause of death in four patients. Six of the seven patients studied developed generalized edema at some stage. These facts emphasize the necessity for rigid restriction of fluid and sodium.

Peritoneal or gastric lavage is used only if the patient shows some deleterious effects from nitrogen retention or electrolyte disturbance, particularly hyperpotassemia.

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GLUCOSE ASSIMILATION DURING ANESTHESIA AND SURGERY*†

MORTON D. PAREIRA, M.D., AND J. G. PROBSTEIN, M.D.

ST. LOUIS, MISSOURI

FROM THE LABORATORY AND DEPARTMENT OF SURGERY, THE JEWISH HOSPITAL, AND THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

SINCE THE STUDIES OF GRAHAM were reported in 1915,[1] surgeons have assiduously striven to amplify the hepatic glycogen reserve of the preoperative patient. This practice, along with that of parenteral glucose administration in the postoperative state, has yielded benefits so manifest that they need not be recounted here.

In addition to its use before and following operation, carbohydrate is sometimes employed parenterally during operation. There has been no consistency in this practice however, and its rationale has not been established. In the course of our current studies[2] it occurred to us that parenteral glucose administration during anesthesia and surgery invokes considerations distinctive unto itself.

It is known that anesthesia produced by ether, chloroform, and many other agents, induces a significant hyperglycemia in laboratory animals and humans.[2, 3, 4, 5, 6, 7] That hepatic glycogenolysis is the source of this hyperglycemia seems evident since it has not been found to occur in Eck fistula or hepatectomized dogs.[5, 9, 10] Added evidence is supplied by the fact that progressive liver sampling in the ether anesthetized dog shows a decreasing glycogen content.[11, 12]

In the light of these observations two considerations of clinical import arise. The first relates to the assimilability of parenterally administered glucose during anesthesia and surgery. Since at this time glycogen is being broken down in the liver at an abnormally high rate, as indicated above, the possibility that exogenously supplied glucose cannot be assimilated in appreciable amounts must be entertained. But, if glucose can be assimilated during anesthesia and surgery, it would seem rational to administer it at such time in order to replenish the hepatic glycogen reserve at the very time when it is being drained. Such considerations would seem especially apropos for those patients who come to operation with any degree of incorrectible liver damage, as such patients can store only relatively small amounts of glycogen in reserve.[13] In the present study we have determined quantitatively the extent of assimilation of parenterally administered glucose during anesthesia and surgery.

OBSERVATIONS

Twenty-four patients undergoing various surgical procedures were given 1000 cc. of 10 per cent glucose in distilled water intravenously during opera-

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tion. Infusions were begun with the onset of surgical anesthesia at the rate of 10 Gm. per hour during the first half hour, and thereafter at the rate of 45 Gm. per hour until completed, in accordance with a method of glucose infusion previously described.[2] In some instances glucose infusion was temporarily interrupted for infusion of whole citrated blood. When the infusion time exceeded the operating time, the infusion was continued uninterruptedly after completion of the operation. Among the patients studied various lesions and surgical procedures were represented, and certain patients with laboratory evidence of disturbed hepatic function were purposefully included. None of the patients presented clinical or laboratory evidence of primary impairment of carbohydrate metabolism. All postoperative urines were collected and quantitative sugar determinations made by the method of Somogyi.[14] The balance sheets showing the amount of glucose that was utilized in the procedure (glucose infused minus glucose excreted in the urine) are recorded in Table I.

RESULTS

As may be seen in Table I, 20 of the 24 patients assimilated over 90 per cent of the glucose infused. The remaining four patients assimilated less than 90 per cent, but even the poorest result was 83.6 per cent. The degree to which glucose was assimilated was not related to the anesthetic agent used, nor did it show any consistent relation to the duration of anesthesia and operation, to the state of general hepatic function, or to the presence of acute localized infection. Patients No. 19 and 20, in spite of unabolished ketosis at the time of surgery, assimilated 87.1 and 97.4 per cent of the infused glucose, respectively. It might be significant that the former patient presented a history suggesting a longer duration of ketosis than the latter. Only four of the 24 patients in this series (17 per cent) presented immediate postoperative ketonuria, whereas 47 per cent of a consecutive series of 200 patients undergoing operative procedures without concomitant glucose infusion did develop ketonuria.

DISCUSSION

As with all biologic processes, energy must be expended by the liver in performance of its various functions. The hepatic glycogen reserve is important primarily to provide this energy, the preferential fuel of the liver being carbohydrate.[15, 16] Fats and proteins are utilized very uneconomically by the liver for fuel. Glycogen, on the other hand, becomes available for oxidation without involving dissipation of energy.[17] When the hepatic glycogen reserve is not of amount sufficient to satisfy the full energy requirements of the liver, ketosis develops and, as is well known, many deleterious accompaniments may be associated with this state.[18] Furthermore, the liver, being a relatively anoxic organ, is dependent upon the combustion of available glycogen as a substitute for this anoxia in carrying on its normal physiologic activity.[15]

That a rich hepatic glycogen reserve has been found of such great benefit to the surgical patient is quite rational in light of these phenomena. Further consideration would logically indicate that this reserve be available not only

TABLE I.

Case	Surgical Pathology	Complicating Pathology	Operation	Anesthesia	Duration of Anesthesia and Surgery	Evidences of Liver Damage	Percent of Glucose Assimilated
1	Carcinoma of breast	None	Radical mastectomy	Cyclopropane-N_2O-O_2	140 min.	None	90.4
2	Chr. cholecystitis	None	Cholecystectomy	Continuous spinal 225 mg. procaine	85 min.	None	96.0
3	Chr. cholecystitis	Arteriosclerotic heart disease with fibrillation; hepatomegaly.	Cholecystectomy	Continuous spinal 300 mg. procaine	80 min.	Present	95.0
4	Chr. cholecystitis Cholelithiasis	None	Cholecystectomy	Continuous spinal 250 mg. procaine	80 min.	None	95.2
5	Chr. cholecystitis Cholelithiasis	None	Cholecystectomy	Continuous spinal 400 mg. procaine	100 min.	None	99.0
6	Chr. cholecystitis Cholelithiasis	Hypertensive cardiovascular disease	Cholecystectomy	Ether-N_2O-O_2	95 min.	Present	95.0
7	Chr. cholecystitis Cholelithiasis	None	Cholecystectomy Choledechotomy	Ether-N_2O-O_2	110 min.	Present	94.7
8	Chr. cholecystitis Cholelithiasis	Recently subsided acute interstitial pancreatitis	Cholecystectomy	Continuous spinal 300 mg. procaine	90 min.	None	83.6
9	Carcinoma of gallbladder	None	Cholecystectomy	Continuous spinal 325 mg. procaine	140 min.	None	97.0
10	Carcinoma of rectum	None	Abdominoperineal resection of rectum	Continuous spinal 350 mg. procaine	140 min.	None	98.5
11	Carcinoma of rectum	None	Abdominoperineal resection of rectum	Continuous spinal 500 mg. procaine	240 min.	None	86.4
12	Carcinoma of recto-sigmoid	Liver metastases	Abdominoperineal resection of rectum	Continuous spinal 250 mg. procaine	145 min.	Present	96.8
13	Pancreatic necrosis with abscess formation	Generalized arteriosclerosis. Mycrocytic anemia	Partial pancreatectomy	Continuous spinal 200 mg. procaine	65 min.	Present	98.1
14	Hyperthyroidism	"Thyroid heart disease"	Hemithyroidectomy (2nd stage)	Ether-N_2O-O_2	90 min.	None	98.0
15	Diffuse non-toxic goiter	None	Thyroidectomy	Ether-N_2O-O_2	95 min.	None	97.6
16	Choledecholithiasis	Marked obstructive hepatitis	Cholecystectomy Choledechotomy	Continuous spinal 350 mg. procaine	180 min.	Present	97.6
17	Choledecholithiasis	Moderate obstructive hepatitis	Choledechotomy	Ether-N_2O-O_2	180 min.	Present	100.0
18	Essential hypertension	Early cardiac damage	Thoraco-lumbar sympathectomy	Ether-N_2O-O_2	150 min.	None	97.6
19	Acute appendicitis	Ketosis	Appendectomy	Spinal procaine 150 mg.	60 min.	None	87.1
20	Acute appendicitis	Ketosis	Appendectomy	Spinal procaine 150 mg.	60 min.	None	97.4
21	Acute appendicitis	None	Appendectomy	Spinal procaine 150 mg.	45 min.	None	97.4
22	Appendiceal abscess	None	Drainage of abscess	Continuous spinal 225 mg. procaine	105 min.	None	90.4
23	Incarcerated inguinal hernia	Partial intestinal obstruction; hypertensive heart disease	Herniorrhaphy	Continuous spinal 200 mg. procaine	65 min.	None	98.2
24	Incisional (ventral) hernia	None	Herniorrhaphy	Ether-N_2O-O_2	103 min.	None	86.0

for the impact of anesthesia and operation, but that it be maintained throughout the postoperative period.

It would therefore seem rational to supply additional glucose as near as possible to the critical period of operative glycogen breakdown, ideally, during operation itself. Such a procedure, however, would be justified only if it could be ascertained that under the given conditions glucose can be assimilated in appreciable amounts. If not, there would be no advantage to this theoretically desirable procedure and, furthermore, the disadvantage of diuresis would obtain. Certain well established observations, previously discussed, make the assimilability of glucose during anesthesia and operation theoretically uncertain.

The observations reported here show that glucose can be assimilated in quite significant amounts during anesthesia and surgery in patients having no abnormalities of carbohydrate metabolism. Such assimilation has been effected in the presence of prolonged anesthesia, extensive surgical procedures, evidence of diminished hepatic function, and mild degrees of ketosis.

We recognize that most well prepared patients coming to operation will carry an adequate hepatic glycogen reserve through the operative period and until postoperative alimentation is begun. However, since the meticulous pre- and postoperative therapy is for the benefit of the poor risk patient, it is in regard to this group that these considerations find their point. The poor risk patients, from the standpoint of carbohydrate metabolism, in addition, of course, to those with specific metabolic derangements are those with degrees of preoperatively incorrectible liver damage. These patients cannot store appreciable glycogen reserves, and when they undergo formidable operations the considerable operative glycogenolysis and difficulties of postoperative alimentation severely drain the previously attained reserve.

SUMMARY

1. Parenteral glucose, administered in accordance with physiologic principles, is well assimilated during anesthesia and surgery.

2. Parenteral glucose alimentation during major operations is advocated to protect the preoperatively attained glycogen reserve. This practice is especially emphasized when there is any degree of preoperatively incorrectible liver damage.

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PROPHYLAXIS OF OVARIAN CANCER*

HAROLD SPEERT, M.D.

NEW YORK, N. Y.

FROM THE SLOANE HOSPITAL FOR WOMEN AND THE DEPARTMENT OF OBSTETRICS AND GYNECOLOGY COLUMBIA UNIVERSITY, NEW YORK, N. Y.

THE PRESENT STUDY is an attempt to assess the possibility of reducing the mortality from ovarian cancer. Although less prominent in its incidence, cancer of the ovary, because of its low cure rate, ranks fourth among the neoplasms responsible for death in women aged 40 years and over. The mortality rate from this cause among white women beyond the first four decades of life was 17.02 per 100,000 U. S. population in 1945. During that year 4,386 women died as a result of cancer of the ovary.**

With the inadequate methods of therapy now available, three theoretical possibilities exist for lightening the shadow cast by this disease. These include public education, routine periodic pelvic examinations, and prophylactic ovariectomy.

Little benefit is to be expected from attempts at public education. One of the outstanding features of ovarian cancer is its insidious course and the notorious absence of symptoms until the disease is well advanced. H. S. Crossen[3] forcefully called attention to the silent nature of ovarian carcinoma in 1942 and R. J. Crossen[4] (1947) has recently re-emphasized the menace of this characteristic. The onset of symptoms is usually indicative of an incurable stage of the malignant process.

Another possible approach to the problem would be the routine pelvic examination of all women at frequent intervals. It is doubtful, however, whether this procedure will ever be applied to more than a small segment of the population. It is uncertain, moreover, to what extent such a routine would increase the proportion of curable cases. Two recent experiences illustrate the difficulty in recognizing early ovarian cancer and the rapidity with which the tumor may grow.

Case 1.—A woman of 45 years had a hysterectomy for myomata associated with menorrhagia. The adnexa appeared grossly normal and were removed only as a prophylactic measure. Histologic examination of the ovaries showed bilateral adenocarcinoma. Seven months later the pelvis was infiltrated with hard masses and the patient died soon thereafter.

Case 2.—A postmenopausal woman of 55 years had a vaginal hysterectomy for prolapse. Pelvic examination was otherwise negative. Four months later she returned with extensive and inoperable carcinoma of the ovary, proved at laparotomy.

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** These figures, furnished by the U. S. Public Health Service, include deaths from cancer of the fallopian tube and parametrium, but the number of such cases is so small as not to affect significantly the statistics.

Accepting the fact that ovarian cancer, once it becomes symptomatic or clinically recognizable, is usually beyond the reach of curative measures, we can anticipate a decrease in the mortality from this disease only by earlier diagnosis or by prophylactic measures. One such approach is currently feasible, namely prophylactic ovariectomy incidental to other operations. Under some circumstances, such as in a postmenopausal woman undergoing hysterectomy, the desirability of prophylactic bilateral oophorectomy is clear-cut and generally accepted. In younger women, however, in whom the cessation of the menstrual function has not yet occurred, castration provides security against ovarian cancer only in exchange for the sacrifice of the still useful endocrine function of the ovaries. Disposition of the ovaries in borderline cases requires individualization.

This problem has been approached through a study of the case histories of the last 260 patients with definite cancer of the ovary in the Sloane Hospital. Attention was focussed on the past surgical history of these 260 patients, to determine the proportion who had had previous pelvic, lower abdominal, vaginal or other relevant operations. This category included operations on the

TABLE I.—*Previous Relevant Operations in 260 Patients with Ovarian Cancer**

	Operations	Per Cent
Lower abdominal operations	52	60
Vaginal operations	27	31
Breast operations	5	6
Radiotherapy	9	10
Exploration of adrenal	1	..

* Total exceeds the 87 operations mentioned in the text since some of the operative procedures were listed in two categories.

breast, because of the close functional relation between this organ and the ovary, pelvic radiotherapy, and a case in which adrenal exploration was performed for a gynecologic complaint (masculinization). These operations present an obligation carefully to evaluate the status of the patient's ovaries, either by direct inspection or by bimanual palpation with the patient anesthetized, and provide an opportunity, if the abdomen is already open, to remove useless or suspect organs.

Among the 260 patients with ovarian cancer were 67 (26 per cent) who had undergone previously 87 such relevant operations. This is a minimum figure and should probably be somewhat higher since several of the charts lacked details of the patient's past history. The operations are grouped and listed in Table I. Fifty-two of them (60 per cent) were lower abdominal operations, in nine of which hysterectomy was performed; twenty-four (28 per cent) were vaginal operations; five (6 per cent) were operations on the breast; and in nine cases (10 per cent) radiotherapy was used, either in the form of intrauterine radium or external roentgen irradiation.

The age of the patients at the time of the original surgical procedure is shown in Table II. Forty-five of these operations (52 per cent) were per-

formed when the patient was aged 40 years or older, and in 17 of these instances (20 per cent) the patient was beyond the fifth decade of life.

It is a striking fact that following 29 per cent of the original operations less than two years elapsed until the subsequent operation for ovarian cancer. This interval was five years or less after 39 per cent of the original operations. The distribution of the time intervals is shown in Table III.

TABLE II.—*Age of Patients at Original Operations*

Age in Years	Patients		
Under 20	4		
20–24	7		
25–29	2		
30–34	15		
35–39	13		
40–44	13		
45–49	15		
50–54	7		
55–59	4		45 (52%)
60–64	4	17 (20%)	
65–69	1		
70–74	1		

Most of the ovarian neoplasms, as expected, were adenocarcinomas, which comprised 92 per cent of the total. The remaining few tumors consisted of two teratomas, a dysgerminoma, a fibrosarcoma, and a gynandroblastoma.

Because of current interest in the possible carcinogenic effects of radiant energy, and for comparison with a similar tabulation of patients with neoplastic disease of the uterine fundus (Speert and Peightal,[13] 1949), a listing has been made of the patients in the present series who had had previous pelvic radiotherapy for conditions presumably unrelated to their eventual ovarian lesions. These cases, nine in number, constitute 3.5 per cent of the entire series. Table

TABLE III.—*Time Interval Between Original Operation and Subsequent Operation for Ovarian Cancer*

Interval in Years	Patients		
Under 1	11	25 (29%)	
1–2	14		
2–3	1		34 (39%)
3–4	4		
4–5	4		
5–10	16		
10–15	14		
15–20	4		
Over 20	19		

IV presents their main features. The patients ranged between 34 and 62 years in age at the time of irradiation, averaging 45.1 years. Five had been treated with intrauterine radium, four with roentgen rays. Their ovarian cancers were discovered between 2½ and 23 years later, the average interval between irradiation and subsequent operation being 9.3 years.

Analysis of the individual cases on which this study is based has brought to light several instances in which conservatism seems to have been overdone, to the detriment of the patient. Some of these cases are abstracted below.

Case 3.—This patient underwent a multiple myomectomy at age 40 years. Because of recurrence of her fibroids, hysterectomy and right salpingo-oophorectomy were performed nine years later, at age 49. Six years later routine physical examination revealed an abdominal tumor, which at operation was found to be a hopelessly extensive carcinoma arising from the left ovary. The patient died a year afterward.

Case 4.—This patient had her right ovary removed because of a cyst at age 50. Eight years later she complained of swelling of the abdomen and legs. She died in uremia while under study. Autopsy revealed a primary cystadenocarcinoma of the left ovary.

Case 5.—This patient had a hysterectomy for fibroids at age 47. Five years later she complained of abdominal pain and vomiting. Exploratory laparotomy revealed an inoperable ovarian carcinoma.

Case 6.—This patient had a curettage at the age of 35 years and another at the age of 39, both for menorrhagia. At the age of 43 hysterectomy and appendectomy were performed, presumably for the same reason. A year later she complained of indigestion,

TABLE IV.—*Ovarian Tumors Following Previous Pelvic Irradiation*

Patient	Age	Irradiation	Dose	Indication	Interval (Years)	Ovarian Tumor
A	46	Radium	?	Menorrhagia	23	Cystadenocarcinoma
B	51	Radium	?	? Cervical cancer	6	Adenocarcinoma
C	46	Radium	1800 mg. h.	Metrorrhagia, functional	5	Cystadenocarcinoma
D	62	Radium	1800 mg. h.	Endometrial polyp	2½	Papillary cystadenocarcinoma
E	40	Radium(2x)	?	Myomata	22	No specimen
F	34	X-ray	7 treatments 45 min. each	Ovarian cyst	2½	Papillary cystadenocarcinoma
G	42	X-ray	Artificial menopause	Myomata	10	Papillary adenocarcinoma
H	36	X-ray	Artificial menopause	Postpartum metrorrhagia	9	Papillary adenocarcinoma
I	49	X-ray	Artificial menopause	?	4	Papillary pseudomucinous cystadenocarcinoma

weakness and swelling of the feet. Exploratory laparotomy showed an inoperable cystadenocarcinoma of the ovary.

Case 7.—This patient had a supravaginal hysterectomy and left salpingo-oophorectomy for fibroids at age 49. Two years later, complaining of abdominal swelling, she was found to have an inoperable pseudomucinous cystadenocarcinoma. Roentgen-ray therapy prolonged her life another year.

Case 8.—This patient had a suspension of the uterus at age 50. Fourteen years later she had a curettage and anterior and posterior colporrhaphy, but there is no record of the examination at that time. A year later she began to complain of abdominal pressure. At operation an adenocarcinoma of the left ovary was found.

Case 9.—This patient had a hysterectomy for fibroids at age 46. Fourteen years later, six months after the onset of abdominal swelling, she underwent laparotomy for a tumor of the left ovary which was diagnosed pathologically as a fibrosarcoma. She died four months later.

A second group of cases illustrates the tragedies which may result from diagnostic errors in the interpretation of pelvic masses in middle aged or elderly women. Two such cases are presented below.

Case 10.—The patient, at age 71, had a curettage because of a brownish vaginal discharge. A hard, fixed, nodular pelvic mass, extending half-way to the umbilicus, was believed to be a myomatous uterus. Ascites developed soon afterward, and four months later the patient returned with inoperable carcinoma of the ovary.

Case 11.—This patient had a curettage for menorrhagia at age 45. A small fixed mass was palpated in the right fornix. The patient died 3½ years later, eight months after operation for a papillary pseudomucinous cystadenocarcinoma of the ovary.

A third category comprises cases in which surgical operations had been performed a short time before the ultimate detection of the ovarian neoplasm, and where careful inspection or palpation of the ovaries at the first procedure might have permitted earlier definitive therapy for the ovarian tumor. Several illustrative cases follow.

Case 12.—This patient had a curettage at age 56 for postmenopausal bleeding, but the tissue obtained was insufficient for diagnosis. Description of the pelvic examination was not recorded. Eight months later she complained of abdominal pain. Laparotomy revealed extensive adenocarcinoma arising from the right ovary.

Case 13.—This patient had an inguinal herniorrhaphy at age 62. She noticed beginning enlargement of the abdomen three months afterward. In another three months she was found to have an inoperable carcinoma of the ovary.

Case 14.—This patient had a radical mastectomy for carcinoma at age 44. A year later she underwent laparotomy because of menorrhagia and a palpable pelvic tumor. Extensive bilateral ovarian carcinoma was present.

Case 15.—This patient underwent a left radical mastectomy for carcinoma at age 50 years. A year later she complained of abdominal pain, when she was found to have a pelvic tumor. At operation this proved to be a "melon-sized" papillary serous cystadenocarcinoma of the left ovary.

Case 16.—This patient had a curettage at age 45 because of menorrhagia. Pathologic report was endometrial hyperplasia. The record of the examination under anesthesia mentioned only a retroverted uterus. A year and a half later, when vaginal bleeding recurred, now with abdominal pain, the patient was found to have a pelvic tumor. At operation this proved to be a cystadenocarcinoma of the ovary. She died of a pulmonary embolus a week after operation.

Case 17.—This patient had an appendectomy at age 48. Sixteen months later she noticed that her abdomen was enlarging. A large inoperable papillary cystadenocarcinoma of the left ovary arose from the pelvis and there was considerable fluid in the abdomen. The patient died six weeks later.

Case 18.—This patient had a laparotomy at age 56 for repair of a vesicovaginal fistula which had resulted from an application of radium to the cervix five years previously. There is no recorded description of the internal genitalia. A year later, complaining of abdominal pain, she was found to have massive ascites secondary to an inoperable pelvic carcinoma, probably primary in the ovary.

Case 19.—This patient, at age 19, complained of secondary amenorrhea, hirsutism, deepening of the voice, decrease in breast size and loss of weight. Examination showed a masculine habitus, hypertrophied clitoris, and palpably normal uterus and adnexa. Following extensive laboratory study, exploration and biopsy of the right adrenal was performed, all showing no significant pathologic change. Three and a half years later her abdomen began to enlarge. A pelvic tumor was now easily palpable. Following its removal it was classified as a gynandroblastoma. Reoperation a year later and radiotherapy failed to halt the malignant process.

DISCUSSION

The tabulations and illustrative case reports presented above permit certain suggestions for the prophylaxis and earlier detection of ovarian cancer. Twenty-six per cent of our 260 patients with malignant tumors of the ovaries had undergone previous operations which permitted either removal of the ovaries at that time or their inspection or palpation with the patient under anesthesia. This figure agrees well with the 21 per cent incidence of previous relevant operations recently reported by Montgomery[11] (1948) in a study of 99 patients with primary ovarian cancer.

It would appear particularly significant that our patients were at least 40 years of age at the time of 52 per cent of the original operations and in 20 per cent of the cases they had already passed their 50th birthday. While few modern gynecologists would subscribe to the radical teaching, espoused a generation ago by Graves, of removing the ovaries in all patients undergoing hysterectomy, there would seem to be little advantage in allowing a woman of 50 years or more to retain her ovaries under circumstances which permit their easy removal.

The lower age limit for prophylactic ovariectomy must remain an individual problem, governed largely by the psychologic status of the patient. There is greater than a one per cent chance that a woman of 40 years will die ultimately of ovarian cancer.* Few women over this age are unwilling to have their ovaries removed incidental to hysterectomy, for example, if the problem is discussed with them beforehand. In unstable or frankly neurotic women, the prospect of an abrupt or premature menopause may well be a reasonable deterrent to such a procedure. The majority of normal women, however, take their climacteric in stride, requiring only a minimum of help from sedative drugs and an understanding physician. Even for the relatively small group of patients for whom endocrine therapy seems necessary, oral estrogens can now meet this need so easily, so effectively, and so economically, as to remove in large measure the fear of the change of life long shared by patient and doctor alike.

Some of the tumors in the present series appeared within so short a time after the original operation as to suggest the possibility at least of their having been present at that time. Twenty-nine per cent of these operations were performed within two years of the subsequent detection of the ovarian cancer and following 39 per cent of the operations the ovarian tumor was discovered within five years. These data reinforce our attitude concerning the desirability of prophylactic ovariectomy when feasible and when acceptable. They permit, furthermore, an enthusiastic endorsement of H. S. Crossen's[3] recommendation that "every opportunity afforded by anesthesia for a minor vaginal operation be utilized to make deep accurate palpation of the ovarian areas." We would extend this recommendation to include vaginal examinations for middle aged or elderly women when anesthetized for other operations as well. Pierce and Slaughter (Cancer, 1: 468–471, 1948) have recently reached a similar conclusion in a study of 100 women with breast lesions who were subjected to

* Based on 1945 Vital Statistics of the United States.

a gynecological survey. Because of the high incidence of pelvic disease in this group of patients they concluded that it was "the duty of the general surgeon to include a pelvic examination in the investigation of every woman with a breast lesion." About 70 per cent of all ovarian neoplasms are malignant in women over age 50 years (Shands and Clark,[12] 1941), and there is no other simple way to detect these silent tumors in their incipiency. Any palpable ovarian enlargement in women of this age group should require laparotomy for its removal. Cases 10 and 11 illustrate the tragedies which may result from misinterpretation of pelvic masses in middle aged or elderly women.

Abundant experimental evidence attests the effectiveness of radiant energy in inducing ovarian tumors, particularly of the granulosa cell type, in mice (Furth and Butterworth,[6] 1936; Traut and Butterworth,[14] 1937; Geist, Gaines and Pollack,[8] 1939; Furth and Boon,[5] 1947; Lorenz, Eschenbrenner, Heston and Deringer,[10] 1947). The clinical literature also cites several cases in which ovarian cancers have appeared in women subsequent to pelvic irradiation for benign conditions (Werner,[18] 1925; Vogt,[16] 1926; Flaskamp,[7] 1930; Traut and Marchetti,[15] 1940; Vogt,[17] 1941; Burnam,[1] 1942; Crossen and Crossen,[4] 1947; Montgomery,[11] 1948; Husslein,[9] 1948). To this group we can add nine additional cases (Table IV). This number constitutes only 3.5 per cent of our patients with ovarian cancer and is significantly less than the 8 per cent incidence of previous pelvic irradiation in patients with malignant tumors of the corpus uteri (Speert and Peightal,[13] 1949). Moreover, only two instances of ovarian cancer have come to light among a total of 958 patients in whom a radiotherapeutic menopause has been induced in this clinic and who were followed for an average of 6.7 years or a total of 6,402 person-years (Corscaden, Fertig and Gusberg,[2] 1946). These facts suggest no relationship between ovarian neoplasms and previous pelvic radiotherapy. In 359 patients (37 per cent), however, the follow-up period was less than two years. Our observations, therefore, are not completely satisfactory since radiant energy requires a long latent period, often 20 years or more, for the manifestation of its carcinogenic effect, even on tissues of known susceptibility such as skin. The question must be regarded as unsettled at present; available data seem to provide no clear evidence that radiant energy is carcinogenic for the human ovary.

SUMMARY

1. A significant proportion of ovarian cancers can be prevented by routine ovariectomy in women undergoing pelvic laparotomy. This prophylactic measure is recommended for most patients over 40 years of age.

2. Among 260 consecutive patients with primary ovarian cancer 26 per cent had had previous relevant operations. These included surgical procedures involving the pelvis, lower abdomen, vagina and breast, and pelvic radiotherapy. The patients were 40 years or older at the time of 52 per cent of the original operations and in 20 per cent they were aged 50 or more. The ovarian tumors were discovered within two years of 29 per cent of the original operations.

3. It is recommended that every opportunity be utilized for pelvic examination under anesthesia of all middle aged or elderly women and that all palpable adnexal masses in postmenopausal women be considered an indication for exploratory laparotomy.

4. No causal relationship was found between irradiation and human ovarian cancer.

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RATIONALE OF THERAPY IN ACUTE VASCULAR OCCLUSIONS BASED UPON MICROMETRIC OBSERVATIONS*†

WAYNE B. MARTIN, M.D., HAROLD LAUFMAN, M.D., PH.D.,
AND
STANLEY W. TUELL, M.D.

CHICAGO, ILL.

FROM THE DEPARTMENT OF SURGERY, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

IN A PREVIOUS COMMUNICATION we have described our technic for measuring the changes in caliber of the small vessels of a vascular tree following main stem occlusion.[12] All observations were made on mesenteric vessels using a Kniseley fused quartz rod trans-illumination apparatus employing a constant temperature tissue bath with variable volume flow. Young, small dogs were used and intravenous nembutal anesthesia was employed. A special lucite tray held the dog's mesentery in a nonstretched position, submersed in constantly circulating mammalian Ringer's solution at body temperature. The microscope was fixed on small vessels. A small precapillary artery and vein running side by side were chosen for observation, the artery measuring from .054 to .144 mm. in the various animals and the vein from .090 to .288 mm. We found that the behavior of small arteries and veins followed more or less constant patterns of change in caliber pursuant to a main stem occlusion and after its release. For purposes of orientation, these patterns will be reviewed briefly.

Following clamping of the superior mesenteric artery, both the small artery and vein under observation diminished in caliber. After release of the occlusion the small artery remained in moderate spasm for a short period of time before returning to the control caliber. This phenomenon we termed residual vasospasm. It occurred in the presence of grossly visible reactive hyperemia of the involved intestine.

Following clamping of the superior mesenteric vein, the small veins became dilated, while the small arteries exhibited a marked diminution in caliber. After release of the venous occlusion, temporary residual vasospasm in the small artery was again noted. As the artery returned to its control caliber, the engorged vein also regained its control diameter.

These patterns were demonstrated in 110 observations on 61 animals. The only differences which occurred were in the extent of change; the pattern seemed constant. We have termed the diminutions in caliber "spasm" because of certain evidence to substantiate the use of this term. Further evidence to support this viewpoint is presented in this paper.

The purpose of this report is to describe the variations imposed on these patterns by the actions of certain therapeutic measures in common use today.

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All our observations were made by direct microscopic measurement, using a Leitz micrometer installed into the lens system of the microscope. Since we employed direct micrometry, we felt that we might be able to furnish direct evidence pertaining to the influence of various forms of therapy on vessel caliber in acute vascular occlusions. Much of the therapy in vogue today is still controversial, as evidenced by conflicting reports in the literature over the past ten years. Further, there is confusion concerning basic vascular physiology following vascular occlusions. This situation probably exists because most of the conclusions have been arrived at by indirect measurements.

To illustrate one phase of this problem—the question of the existence of venospasm following venous occlusion or thrombophlebitis—we should like to quote from some of the most recent authors.

Allen, Barker and Hines in their recent book on peripheral vascular disease[1] have said:

> "There seems to be some disagreement with regard to the incidence of arteriospasm in cases of ileofemoral thrombophlebitis. It certainly occurs in occasional cases during the acute phase of the disease and may be so severe that pulsations in the larger arteries disappear for several hours after the clinical onset of the disease. Although some data indicate sympathetic innervation of veins, the theoretic possibility of spasm of venules in cases of ileofemoral thrombophlebitis is not supported by clinical evidence. It is extremely difficult to understand how spasm of the venules can take place in the presence of intense congestion and obvious distention of small veins."

In his investigations on venospasm, de Sousa Pereira[7] has indicated that venospasm following thrombophlebitis is responsible for much of the pain. Sympathetic block resulted in relief from venous pain for a period longer than the anesthetic action of the drug employed. This suggested that venospasm may play an important role in the mechanism of pain under such conditions. This author also demonstrated active constriction in the veins in thrombophlebitis. In a recent review, White[18] has stated:

> "The importance of sympathetic innervation of the veins is still uncertain. While numerous nerve fibers are present in their walls, it is not known how active a role they play in regulating their caliber. Definite dilatation of the veins of patients with thrombophlebitis is clearly shown in contrasting venograms taken before and after procaine block. This clear demonstration of increased venous flow, although most convincing evidence of the therapeutic value of procaine block, does not prove that the increased diameter of the veins is due to release of spasm in their walls. Exactly the same result would follow increased arterial inflow and secondary distention."

However, White reports that de Sousa Pereira illustrated an increase in caliber of the internal saphenous vein in phlebograms taken before and after the intravenous injection of procaine in a single patient. White comments, "This should not have increased arterial inflow, and, therefore, constitutes fairly convincing evidence that a certain degree of active neurogenic venous constriction may be present."

In our experiments reported below we measured the caliber of the small vessels following venous occlusion and arterial occlusion in the presence of sympathectomy and compared these measurements with the control pattern. In other experiments we utilized oxygen, papaverine and tetraethylammonium chloride, and made comparable measurements. Observations were also made on the effects of anticoagulants.

We wish to emphasize that our measurements represent vessel caliber only, and no attempt is made in this report to correlate vessel caliber with local blood flow, local blood pressure, local pulse volume or local temperature.

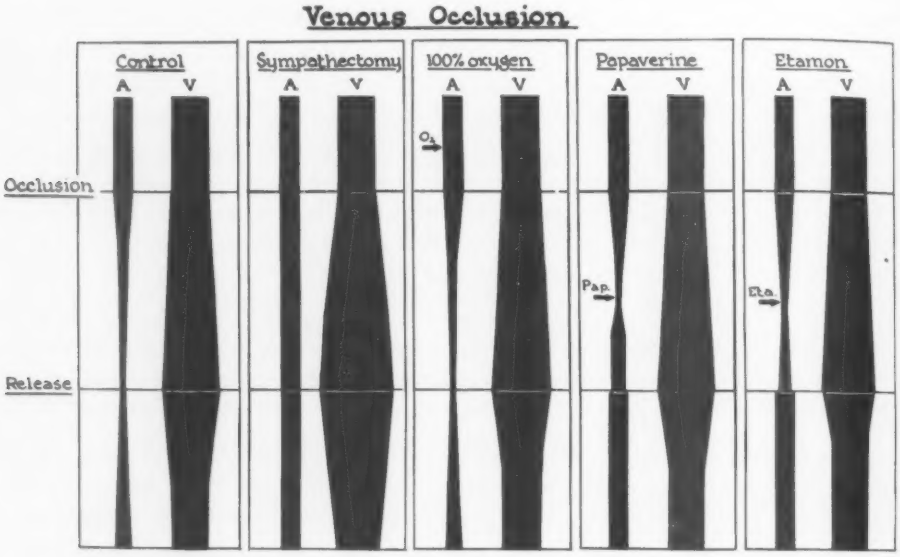

FIG. 1.—Micrometric pattern of responses in small vessel caliber following acute venous occlusion with various forms of therapy. *Control:* After occlusion of main stem vein, the artery (A) goes into reflex spasm while the vein (V) becomes moderately dilated. Upon release of the occlusion, there is a period of residual spasm in the artery while the vein returns to pre-occlusion caliber. *Sympathectomy* abolishes all reflex arterial spasm as well as the residual arterial spasm following release of the occlusion. The vein becomes dilated to a diameter exceeding that of the control during occlusion. *100% oxygen* has no effect on the pattern of vasospasm in venous occlusion (compare with control). *Papaverine*, given during reflex arterial spasm, abolishes some of the spasm. After release of the occlusion there is no phase of residual spasm. *Tetraethylammonium Chloride* (*Etamon*), given during reflex arterial spasm abolishes some of the spasm in only 50% of cases (cross-hatched area). After release of the occlusion there is no phase of residual spasm. (See text for further details.)

EFFECT OF SYMPATHECTOMY ON VESSEL CALIBER IN ACUTE VENOUS OCCLUSION

Technic. Since all our observations were made on mesenteric vessels, local sympathectomy could be accomplished by the simple expedient of stripping the main stem of the superior mesenteric vessels. It is known that the sympathetic nerves to the mesenteric vascular tree follow the main stem vessels instead of entering the branches in a segmental manner as in the extremities. Occlusions were produced by placing a rubber-tipped clamp on the superior mesenteric

TABLE I.—*Comparison of Typical Responses in Small Vessel Caliber After Venous Occlusion in Control and Sympathectomized Vessels*

	CONTROL				SYMPATHECTOMY			
	Dog No. 14				Dog No. 66			
	Artery		Vein		Artery		Vein	
	Caliber	Per Cent	Caliber	Per Cent	Caliber	Per Cent	Caliber	Per Cent
Pre-occlusion reading.....	.090 mm.	100%	.162 mm.	100%	.054 mm.	100%	.108 mm.	100%
50 min. after venous occlusion	.036 mm.	40%	.180 mm.	111%	.054 mm.	100%	.144 mm.	133%
5 min. after release of venous occlusion	.063 mm.	70%	.162 mm.	100%	.054 mm.	100%	.144 mm.	133%
55 min. after release of venous occlusion	.090 mm.	100%	.162 mm.	100%	.054 mm.	100%	.126 mm.	117%
Summary:	Maximum decrease in caliber of artery following venous occlusion: 40% of pre-occlusion caliber.		Maximum increase in caliber of vein following venous occlusion: 111% of pre-occlusion caliber.		No change in caliber of artery following venous occlusion.		Maximum increase in caliber of vein following venous occlusion: 133% of pre-occlusion caliber.	

vein. The controls for this experiment consisted of 33 venous occlusions in unsympathectomized dogs, reported in our previous communication. After a control period of observation of about one hour, venous occlusions were made lasting from 30 minutes to one hour 30 minutes. Post-release observations were made up to 2 hours 15 minutes.

Results. Occlusion of the denervated superior mesenteric vein was carried out in 10 dogs. In no instance did occlusion result in spasm of the small arteries. This finding was in direct contrast to the uniform production of arterial vasospasm which occurred following venous occlusion in the intact specimens.

The small veins in the control series were always moderately dilated following venous occlusion. In the sympathectomized animals, this dilatation was appreciably magnified.

Discussion. It appeared that when the nerve fibers were stripped from the vein, reflex vasospasm in the concomitant arterial tree no longer occurred. This would support the evidence that the sympathetic fibers associated with veins carry afferent impulses. The fact that there was an additional dilatation of the veins following venous occlusion when the nerves were severed, implies that considerable tonus exists in venous occlusion, despite the dilatation by back pressure. It is our impression that when the efferent impulses responsible for this tonus can no longer reach the vein wall, additional dilatation is permitted. There is no reason to assume the venous pressure in sympathectomized occluded veins is any different from that in intact occluded veins. This finding indicates, then, that the sympathetic fibers of veins normally carry efferent impulses also. Furthermore, in venous occlusions, the question of whether actual venospasm exists seem dependent upon a balance of two opposing forces: (1) the ability of the vein to contract on stimulation of its nerve fibers by the occlusive irritant, and (2) the pressure head of the blood in the blocked venous system. Because of the thin muscular coat of these vessels, the latter outbalances the former.

It can be inferred from our measurements that interruption of the sympathetic fibers is of value in increasing the caliber of the concomitant arterial tree in acute venous occlusions. The fact that sympathetic denervation allows a greater dilatation of an already dilated venous tree might imply a state of increased tonus in the presence of acute venous occlusion, which tonus is released upon denervation.

EFFECT OF SYMPATHECTOMY ON VESSEL CALIBER IN ARTERIAL OCCLUSION

Technic. The controls for this series consisted of arterial occlusions made on 21 dogs reported previously.[12] The main stem of the superior mesenteric artery was stripped of its adventitia and the rubber-tipped clamp was placed in this area after a period of control observation as described above. Arterial occlusions were made lasting from 5 minutes to 64 minutes.

Results. Occlusion of the denervated mesenteric artery was carried out in 14 dogs. The pattern of behavior of the small vessels consisted of no change in caliber of either the artery or vein during the period of occlusion as compared to the pre-occlusion caliber. This was in contrast to the repeated observation of severe spasm in the small artery and moderate spasm in the small vein following arterial occlusion in the unsympathectomized animals.

Upon release of the occlusion there was also no change in caliber of the artery or vein in 9 (64.2 per cent) of the animals. In the remaining 5 animals (35.8 per cent) there was a fleeting period of actual dilatation in the small arteries immediately following release of the arterial occlusion.

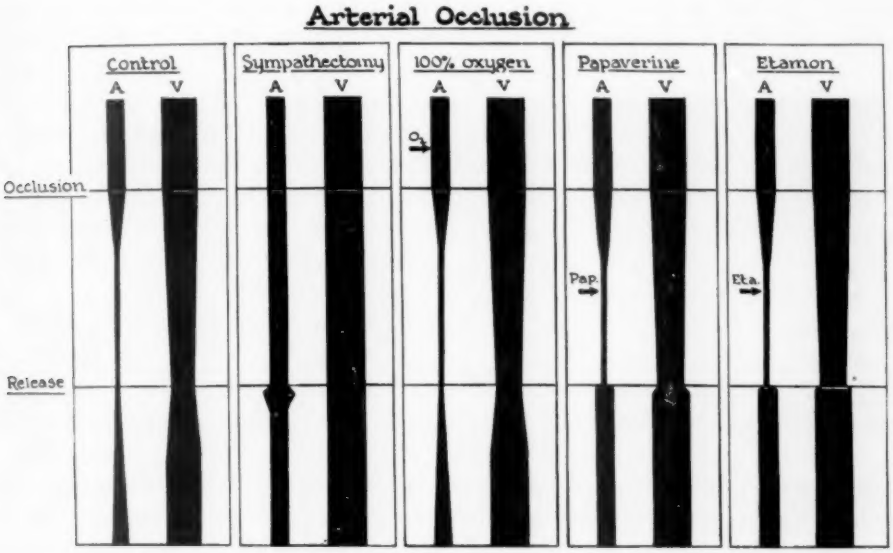

FIG. 2.—Micrometric pattern of responses in small vessel caliber following acute arterial occlusion after various forms of therapy. *Control:* After occlusion of the main stem artery, the artery (A) goes into marked spasm while the vein (V) exhibits a mild degree of spasm. Upon release of the occlusion, there is a period of residual spasm in the artery and a similar period in the vein. *Sympathectomy* abolishes all spasm in both artery and vein, during occlusion as well as after release. In some cases, reactive hyperemia is reflected in the caliber of the small artery after release of the occlusion. (Cross-hatched area.) *100% oxygen* has no effect on the pattern of vasospasm in arterial occlusion. *Papaverine,* given during arterial occlusion, has no effect on arterial spasm. After release of the occlusion, the drug abolishes residual spasm. *Tetraethylammonium Chloride* (*Etamon*), given during arterial occlusion has no effect on arterial spasm. After release of the occlusion, the drug abolishes residual spasm. (See text for further details.)

Discussion. The fact that there was no diminution in caliber of the small arteries following arterial occlusion in sympathectomized specimens indicates that arterial caliber is not altogether dependent upon blood flow. On the contrary, arterial caliber seems dependent mainly on sympathetic control. In both the control and the sympathectomized animals the artery was completely occluded, and the inflow of arterial blood was reduced to zero in each case.

TABLE II.—*Comparison of Typical Responses in Small Vessel Caliber After Arterial Occlusion in Control and Sympathectomized Vessels*

	CONTROL				SYMPATHECTOMY			
	Dog No. 23				Dog No. 16			
	Artery		Vein		Artery		Vein	
	Caliber	Per Cent	Caliber	Per Cent	Caliber	Per Cent	Caliber	Per Cent
Pre-occlusion reading.....	.072 mm.	100%	.135 mm.	100%	.090 mm.	100%	.180 mm.	100%
60 min. after arterial occlusion	.018 mm.	25%	.090 mm.	67%	.090 mm.	100%	.180 mm.	100%
5 min. after release of arterial occlusion	.054 mm.	75%	.108 mm.	86%	.090* mm.	100%	.180 mm.	100%
20 min. after release of arterial occlusion	.072 mm.	100%	.135 mm.	100%	.090 mm.	100%	.180 mm.	100%
Summary:	Maximum decrease in caliber of artery following arterial occlusion: 25% of pre-occlusion caliber.		Maximum decrease in caliber of vein following arterial occlusion: 67% of pre-occlusion caliber.		No change in caliber of artery following arterial occlusion.		No change in caliber of vein following arterial occlusion.	

* In 36% of cases there was a fleeting increase in caliber up to 120% of pre-occlusion caliber immediately after release.

Diminution in caliber occurred when the nerves were intact, but was absent when the nerves were cut. Consequently it would appear that this response is an active one and dependent more upon the stimulation of the sympathetic reflex arc than it is upon the pressure gradient within the vessels. We therefore feel justified in terming the diminution in caliber *spasm*. If the caliber of the vessel were solely dependent upon blood flow within it, this term would not be justified.

Upon the release of an arterial occlusion in a sympathectomized vessel there may be a period of actual dilatation in about 1/3 of the cases. This dilatation is concurrent with the period of reactive hyperemia. Thus the spasm of small arteries during reactive hyperemia in non-denervated specimens appears to be a compensatory mechanism under the influence of sympathetic control. In the experiments of Eichna and his co-workers[8] it was found that reactive hyperemia was observed after sympathectomy, but no comment was made as to the extent. The results of our experiments indicate that after sympathectomy, reactive hyperemia might actually be increased in extent.

In summary, our experiments with acute arterial and venous occlusions with and without sympathectomy have indicated that there are afferent as well as efferent fibers in both arteries and veins, and that these fibers are largely responsible for the patterns of response following occlusions. In venous occlusions the pressure gradient of blood flow appears to play a predominant role in deciding the caliber of the small veins, since these vessels are thin-walled and probably do not carry a very heavy sympathetic innervation. On the other hand, the pressure gradient of blood flow in arterial occlusions appears to play a secondary role to the presence or absence of sympathetic stimulation of the arterial tree.

Although it is hazardous to draw parallels too closely between experimental observations and clinical implications, it would appear that the rationale for sympathectomy or sympathetic procaine block in acute venous occlusions is based primarily on the release of reflex arterial spasm.

In acute arterial occlusions, sympathectomy eradicates vasoconstrictor impulses and thereby prevents vasospasm. However, a direct clinical application of this fact may occasionally be fraught with danger. For example, if sympathectomy is performed on a patient whose limb is precariously surviving following an acute arterial occlusion, surgical sympathectomy may reduce blood pressure temporarily, sufficient to endanger the survival of the limb. Two such cases were recently demonstrated.[17] It might be better to apply our findings in such cases as an indicator for repeated procaine blocks to paralyze the sympathetic ganglia, rather than for surgical extirpation. In less crucial instances, sympathectomy would seem to be indicated. A limb which has been the seat of chronic vascular disease for a considerable period of time prior to acute occlusion may benefit more from sympathectomy than an otherwise normal limb suddenly deprived of most of its blood supply.

Sympathectomy directly releases vasospasm, but has only an indirect effect on blood flow. We have observed microscopically several instances in which the rate of flow actually appeared slower following sympathectomy than it did

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before. The rate of flow bore neither a direct nor inverse relationship to vessel caliber but seemed to depend mainly on other factors, such as blood pressure.

Upon the removal of an occlusion from a sympathectomized vessel, there was no phase of residual vasospasm. This would seem to substantiate the use of repeated sympathetic blocks after embolectomy.

EFFECT OF OXYGEN THERAPY ON VESSEL CALIBER IN ACUTE VENOUS AND ARTERIAL OCCLUSIONS

Technic. One hundred per cent oxygen was administered by intratracheal catheter to eight animals with main stem vascular occlusions. Four were arterial occlusions and four were venous occlusions. In three of the animals (two arterial, one venous) the oxygen was begun before the occlusion. In three (two venous, one arterial) the oxygen was given simultaneously with the release of the occlusion. In two (one arterial, one venous) oxygen was begun just after the occlusion was made.

Results. In no instance did oxygen produce an observable effect on the expected responses in vessel caliber during or after release of the occlusion whether it was arterial or venous. The pattern of response in the small vessels was identical with that in the animals which received no oxygen.

Discussion. Some 20 years ago Chase[4] suggested the use of oxygen inhalation as a therapeutic measure in the revival of strangulated intestine. Recently this method was again advocated for the recognition of viability in a loop of bowel whose circulation had been impared, as well as a form of therapy for the revival of such a segment.[14] Our reason for performing this experiment arose from the fact that for many years physiologists have found that oxygen is of no value in the type of anoxia distal to a vascular occlusion (stagnant anoxia). Our observation that oxygen had no direct effect upon the pattern of vasospasm during or after acute vascular occlusions seemed to be at variance with the findings of the recent writers. This discrepancy can probably be explained by the assumption that the improvement in color of released strangulated bowel by oxygen inhalation occurred because the patients were under the influence of inhalation anesthesia. The diminution in oxygen intake under such conditions would result in a state of anoxic anoxia of a moderate degree. Hence in such clinical instances there could be superimposed upon the stagnant anoxia of occlusion, a state of anoxic anoxia. It is well known that the administration of oxygen is beneficial in states of anoxic anoxia. However, this increased oxygenation of the blood flowing to a given part apparently has no bearing upon the caliber of the vessels in that part. A further beneficial effect upon local circulation might perhaps be attributed to better oxygenation of the heart muscle[19] inducing it to improve the general circulatory status of the patient.

Thus our findings indicate that oxygen therapy has no effect in dilating the vessels of tissues which have been released from vascular occlusions. An improvement in the oxygenation of such tissues might be seen in instances in which there has been a state of anoxic anoxia superimposed. Oxygen appears to have no direct effect upon vessel caliber during or after stagnant anoxia.

EFFECT OF PAPAVERINE HYDROCHLORIDE ON VESSEL CALIBER IN ACUTE VENOUS AND ARTERIAL OCCLUSIONS

Technic. Papaverine hydrochloride was administered by slow injection into a peripheral vein using ½ grain doses for dogs weighing about 5 kilograms. The drug was administered at the height of arterial vasospasm during the occlusions.

Results. (1) VENOUS OCCLUSIONS. Papaverine hydrochloride was administered to six animals during venous occlusion. It had a moderate effect in all animals, releasing some, but not all, of the spasm in the small arteries. The drug had no effect if given after the blood had ceased flowing through the small arteries. Once thrombosis of the small vessels occurred, the drug had no effect. The dilating effect of the drug became more pronounced upon release of the occlusion, eradicating the phase of residual spasm which would have otherwise occurred.

(2) ARTERIAL OCCLUSIONS. In none of six instances was papaverine found to have an effect on the caliber of the small arteries during arterial occlusion. In two instances of arterial occlusion the injection of papaverine was followed by an increase in the *rate* of flow in the arterial bed in the microscopic field, but there was no effect on the caliber of the vessels. At the conclusion of these two experiments further dissection at the site of application of the occluding clamp revealed that there existed a small collateral vessel proximal to the point of occlusion in each instance.

Once an arterial occlusion was released, papaverine eradicated the phase of residual spasm.

Discussion. Papaverine hydrochloride is a drug which apparently acts directly on the muscle fiber within the muscle wall.[6] Its action is not dependent upon the integrity of the sympathetic nerves. Laufman and Method[13] have indicated that there was a definite gross color response to therapeutic doses of papaverine following the release of a still viable loop of bowel from strangulation. Our present observations indicate that the drug is of some value in releasing reflex arterial spasm in acute venous occlusions, providing the drug is used before thrombosis of the smaller vessels becomes widespread. It is also of value in obliterating the phase of residual vasospasm following release of vascular occlusion of either the arterial or venous type. The drug is of no value in acute arterial occlusions except when there are collateral vessels proximal to the occlusion which might be dilated sufficiently to carry an additional blood supply to the part. Concerning this point we believe that the collateral vessels in the vicinity proximal to an occlusion respond to the occlusive irritant by reflex spasm at the time of occlusion. Once the vasodilating effect of papaverine is exerted, the collateral vessels can carry a larger load. This could account for the increased rate of flow in the vessels under the microscope in the two cases cited above.

It would appear, therefore, that papaverine should continue to serve as a useful adjunctive treatment in clinical instances of acute venous and arterial occlusions. In venous occlusions it will release some of the reflex vasospasm in

TABLE III.—*Typical Responses in Small Vessel Caliber After Venous and Arterial Occlusion in Animals Treated with Papaverine Hydrochloride at Height of Vasospasm.*

VENOUS OCCLUSION				
Dog No. 89				
	Artery		Vein	
	Caliber	Per Cent	Caliber	Per Cent
Pre-occlusion reading.....	.054 mm.	100%	.099 mm.	100%
28 min. after venous occlusion	.018 mm.	33%	.117 mm.	118%
40 min. after venous occlusion and 10 min. after papaverine I. V.	.040 mm.	83%	.117 mm.	118%
5 min. after release of venous occlusion	.054 mm.	100%	.099 mm.	100%
55 min. after release of venous occlusion	.054 mm.	100%	.099 mm.	100%
Summary:	Papaverine induced a partial relief of arterial vasospasm in venous occlusion and eradicated residual vasospasm after release of occlusion.			

ARTERIAL OCCLUSION				
Dog No. 80				
	Artery		Vein	
	Caliber	Per Cent	Caliber	Per Cent
Pre-occlusion reading.....	.072 mm.	100%	.144 mm.	100%
25 min. after arterial occlusion	.036 mm.	50%	.126 mm.	87.5%
40 min. after arterial occlusion and 10 min. after papaverine I. V.	.036 mm.	50%	.126 mm.	87.5%
8 min. after release of arterial occlusion	.054 mm.	75%	.126 mm.	87.5%
40 min. after release of arterial occlusion	.072 mm.	100%	.144 mm.	100%
Summary:	Papaverine had no observable effect on pattern of vasospasm in arterial occlusion.			

the small arteries providing it is used before the blood flow in these vessels becomes arrested. In arterial occlusions its value will depend upon the presence or absence of collateral arteries to the part. In either case it should be valuable in eradicating residual vasospasm following removal of an occlusion (*i.e.*, following embolectomy).

EFFECT OF TETRAETHYLAMMONIUM CHLORIDE (ETAMON) ON VESSEL CALIBER IN VASCULAR OCCLUSIONS

Technic. Tetraethylammonium chloride was administered by slow injection into a peripheral vein using from ½ to 1 cc. of the drug for dogs weighing about 5 kilograms. The drug was administered at various stages of arterial vasospasm during both venous and arterial occlusions. It was found that this drug had to be injected very slowly in order to obtain a therapeutic effect. If it was injected too rapidly there was a reversal of effect which will be described below.

Results. (1) VENOUS OCCLUSIONS. In 19 main stem occlusions we found that tetraethylammonium chloride was able to release the reflex arterial spasm in 10 (53 per cent) of the animals. In these animals the drug was injected equally slowly and therefore we consider these findings valid. In three of the nine remaining animals arterial spasm was uneffected during the occlusion, while in six there was a slight but insignificant response. Upon release of the occlusion in the entire group, the phase of residual spasm was usually eradicated. In one instance the drug was injected immediately upon release of the occlusion with an equivocal result.

Once the shock state became obvious, the drug was found to have no effect on the caliber of the vessels. Moreover, if the drug was injected too rapidly the small vessels exhibited a striking degree of vasospasm within a few minutes. This spasm persisted for as long as 30 minutes or until the animal recovered from the shock state. None of the animals exhibiting this reversal of effect are included in the figures quoted above. As was the case when other therapeutic measures were employed, no effect was noted if tetraethylammonium chloride was injected after circulation in the small vessels became arrested.

(2) ARTERIAL OCCLUSIONS. In no instance of eight arterial occlusions was tetraethylammonium chloride successful in releasing the state of arterial spasm. No collateral vessels existed in any of these cases. Once the occlusions were removed, however, the phase of residual spasm was usually eradicated.

Discussion. Since the original claims of Berry and associates[2, 15] were published, several controversial reports[5] have appeared in the literature. The action of the drug is that of an autonomic blocking agent. It has been suggested[10] that the effect of this drug is roughly proportional to the degree of vasoconstrictor tone and that the magnitude of the response is greater in cases in which the tonus is increased. This concept is apparently tenable where the tonus throughout the entire body is of almost equal magnitude. Deductions from our observations would indicate that this concept must be revised when

TABLE IV.—*Typical Responses in Small Vessel Caliber After Venous and Arterial Occlusion in Animals Treated with Tetraethylammonium Chloride at Height of Vasospasm.*

VENOUS OCCLUSION

Dogs Nos. 78* and 95†

	Artery				Vein			
	Caliber		Per Cent		Caliber		Per Cent	
	Dog No. 78	Dog No. 95	Dog No. 78	Dog No. 95	Dog No. 78	Dog No. 95	Dog No. 78	Dog No. 95
Pre-occlusion reading.....	.072	.090	100%	100%	.180	.144	100%	100%
20 min. after venous occlusion	.036	.045	50%	50%	.216	.180	120%	125%
40 min. after venous occlusion and 10 min. after Etamon I. V.	.040	.081	55%	90%	.216	.180	120%	125%
5 min. after release of venous occlusion	.054	.090	75%	100%	.216	.162	120%	112%
30 min. after release of venous occlusion	.072	.090	100%	100%	.180	.144	100%	100%

Summary: Tetraethylammonium chloride released arterial vasospasm and eradicated residual vasospasm in 53% of cases of venous occlusion. In 47% of cases the drug had an insignificant effect.

* Representing 47% of animals in this group.
† Representing 53% of animals in this group.

ARTERIAL OCCLUSION

Dog No. 108

	Artery		Vein	
	Caliber	Per Cent	Caliber	Per Cent
Pre-occlusion reading.....	.072	100%	.162	100%
50 min. after arterial occlusion	.045	60%	.108	67%
62 min. after arterial occlusion and 10 min. after Etamon I. V.	.045	60%	.108	57%
5 min. after release of arterial occlusion	.063	88%	.162	100%
30 min. after release of arterial occlusion	.072	100%	.162	100%

Summary: Tetraethylammonium chloride had no observable effect on pattern of vasospasm in arterial occlusion when no collateral vessels were present.

applied to local stimulation of vasoconstrictor fibers, as occurs in acute vascular occlusions. We conceive that the drug, by acting upon all ganglia in the body, has a lesser effect upon those ganglia harboring a powerful stimulus from an occlusive irritant than it would have upon normal ganglia. This, in effect, would be a distribution along "paths of least resistance." Thus, in an instance of acute vascular occlusion the action of the drug would dissipate itself throughout the body without being able to "break through" the area in which it was most needed. If its action resulted in a general drop in blood pressure, a harmful effect might result in the area already suffering from a diminished blood supply. If the drug is injected too rapidly and a lowering of the blood pressure ensues, the same effect might result. This was reflected in our measurements by an actual diminution in caliber of already spastic vessels.

In venous occlusions where the afferent stimulation is apparently not very great, we found that the drug has a beneficial effect in approximately 50 per cent of cases. However, in arterial occlusion where there is a much stronger afferent stimulation, the drug in therapeutic doses was not able to induce an increase in caliber of the vessels concerned. When collateral circulation is available the drug apparently has a favorable effect in dilating these channels,[9] especially if the vessel is sectioned surgically, thus eliminating the presence of an occlusive irritant. In such a case the afferent stimulation of an occlusion-in-continuity is not present. In our arterial occlusions no collaterals existed and the occlusive irritant (clamp) persisted. We feel that our observations on the use of this drug in acute vascular occlusions might help to explain some of the paradoxical effects found in clinical experiences with the use of this drug. A recent report from Mayo Clinic (3) can be interpreted to bear out our concept of the action of this drug in acute vascular occlusion. In this report the drug was found to have a more lasting effect in lowering blood pressure after a Smithwick sympathectomy than it was possible to obtain before the operation, perhaps indicating that a stronger paralyzing effect from a given dose of the drug can be exerted when there are fewer ganglia remaining upon which the drug can act.

The clinical efficacy of tetraethylammonium chloride will depend on the several factors mentioned above.

EFFECT OF ANTICOAGULANTS IN ACUTE VASCULAR OCCLUSIONS

We observed that vasodilating agents could exert their effects on small vessels only when these vessels were free of thrombosis. Although thrombosis did not appear uniformly throughout the small vessel bed, the vessels thus involved would no longer respond to therapeutic measures. Further, we found that we could produce "sludge" at will in the small vessels distal to an occlusion within a relatively short time. We therefore performed a controlled experiment, reported in a previous communication,[11] to investigate the effects of anticoagulants on sludge formation as well as on thrombus formation. For this experiment, venous occlusions were used exclusively, since the process was usually more gradual than in the arterial occlusions and could be followed more closely. The results will be reviewed here briefly.

The animals were divided into four groups of six dogs each. Group I consisted of untreated controls in which venous occlusions were produced; Group II received heparin after the appearance of sludge formation; Group III received heparin before venous occlusion; the animals in Group IV were given dicoumerol over a period of three days prior to venous occlusion.

Our observations indicated that sludged masses of blood cells serve as a matrix for thrombus formation, provided the other conditions favoring thrombosis are present. When anticoagulants are administered in doses known to be clinically effective, yet comparatively safe, thrombosis does not generally occur in the small vessels distal to an occlusion, but such doses do not prevent the formation of sludge.

It appears that the administration of anticoagulants prevents thrombus formation in the presence of sludge by preventing the sludged masses of cells from becoming adherent to the endothelial lining of the vessel. Although anticoagulants may cause some diminution in the tenacity of the adherence of the blood cells to one another, sludge formation, as such, is not prevented.

When heparin was used in conjunction with vasodilating measures, the effects of the latter on vessel caliber were not noticeably magnified, but thrombosis in small vessels was delayed. This allowed the vessels to remain patent. If a vasodilating measure exerted an effect, such an effect was noted only in vessels which were patent.

We were struck by the fact that sludge formation usually appeared within 10 to 20 minutes following a venous occlusion, and thrombus formation was noted in some of the small vessels, especially in the capillaries and venules as early as 30 minutes after the appearance of sludge. The importance of early anticoagulant therapy in occlusive vascular states therefore appears obvious.

DISCUSSION

There has been some discussion in the recent literature concerning the interpretation of attempts at generalized vasodilatation as a therapeutic measure in localized vascular disease. DeBakey and co-workers[5] have revived the "borrowing-lending" phenomenon as an explanation for the behavior of the blood in the presence of localized vasodilatation. They found that tetraethylammonium chloride was unable to relieve pain-induced local vasospasm because the generalized effect of the drug did not result in the shifting of blood to the affected part. The time-honored principle that blood shifts back and forth from one part of the body to the other depending on local needs has been labeled by these authors, "hemometakinesia." Regarding the use of vasodilators within the scope of this concept, they have said:

> "Indeed, we have yet to find a general vasodilator which could produce in a local part, such as the toes, fingers, foot, hand or extremity, vasodilatation equal in degree or duration to that produced by sympathetic denervation of this part."

Our observations and measurements support this statement. It is our impression that the active release of a given vasospastic impulse is the primary

feature while the flow of blood into a now larger vascular bed is the secondary feature. Drugs with generalized action like tetraethylammonium chloride acting upon the ganglia or papaverine acting on the periphery, are each considerably weaker in total effect in releasing local vasospastic impulses than is the direct paralysis of the nerves by procaine. However, tetraethylammonium chloride is able to overcome certain mild local vasospastic impulses despite its generalized activity, such as the reflex spasm in some cases of venous occlusion; thus even if its action results in a lowered blood pressure, the temporary block of the ganglion in question may be all that is necessary in some cases to release the spasm. After this occurs, the increased blood flow might suffice to maintain an improved circulatory status to the part.

We certainly agree with DeBakey and co-workers that in doses large enough to equal the effect of a local sympathetic block, tetraethylammonium chloride is dangerous as a shock-producing drug. Similarly, if papaverine is not injected very slowly, it too, causes untoward effects, such as temporary stimulation of respiration and precipitous drops in blood pressure. We noticed further that tetraethylammonium chloride in excessive doses causes fecal and urinary incontinence. The shock state under such conditions would counteract any beneficial measure obtained by the use of generalized vasodilators. We have observed that generalized vasodilators, whether they act upon the ganglion or upon the vessel wall (provided they can reach this area), are too weak in non-shock-producing doses to overcome vasoconstrictor impulses of great magnitude, but are able to release the relatively weaker impulses in some cases.

SUMMARY

Direct micrometry of small vessel caliber was employed to determine the effects of various therapeutic measures on the pattern of behavior of these vessels following main stem vascular occlusions.

Experiments with sympathectomized specimens indicate that the afferent and efferent fibers of both arteries and veins are largely responsible for the patterns of response following occlusions, while the pressure gradient of blood flow through the vascular tree becomes important only when the spastic impulses are weak enough to be overcome by the intravascular pressure. Such a situation accounts for venous engorgement during venous occlusion in the presence of increased tonus in the vein wall.

Oxygen therapy was found to have no effect on vessel caliber.

Papaverine hydrochloride was found to be of value in releasing some of the reflex arterial vasospasm in venous occlusion if used before thrombosis occurred. In arterial occlusions, the drug was of value only when collateral arteries existed above the occlusion. Once an occlusion was released, the drug was able to eradicate residual spasm in the small vessels.

Tetraethylammonium chloride in non-shock-producing doses was able to counteract the vasospastic effects following acute venous occlusion in only 50 percent of cases, while in acute arterial occlusions it was entirely without value. An interpretation of these findings is offered.

Sludge formation is found to occur within a relatively short time after either

arterial or venous occlusion. This phenomenon appears to be a precursor to thrombosis. Heparin and dicoumerol prevent thrombus formation in such cases, but do not alter the character of sludge appreciably. The fact that vasodilating agents are not capable of producing a favorable effect in thrombosed small vessels, implies that the use of anticoagulants be an integral part of therapy in acute main stem occlusions.

Regional sympathetic denervation eradicates the pattern of small vessel spasm to an extent unequalled by the generalized vasodilators employed. However, once an occlusion is released, such generally acting drugs are usually able to counteract residual vasospasm.

Our evidence indicates that the regulation of arterial caliber following occlusions is primarily an expression of sympathetic stimulation and secondarily that of blood flow.

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THE TREATMENT OF CARBUNCLES BY THE LOCAL INJECTION OF PENICILLIN*

THOMAS H. BATE, M.D.

PHOENIX, ARIZONA

THE PURPOSE OF THIS PAPER is to present the results of a new method in the treatment of carbuncles. The true carbuncle with extensive involvement of the subcutaneous tissue and multiple draining sinuses through the underlying skin presents a surgical problem of major importance. A great many patients suffering from carbuncle are also the victims of diabetes, nephritis, or other debilitating diseases, which on occasion complicate the management and must be treated along with the carbuncle. Carbuncles have been treated by such methods as hyperemia, as suggested by Bier,[1, 2] injection of antiseptics into their centers,[3] ointments,[4] vaccines,[5] injection of autogenous blood,[6] roentgen-ray therapy,[7, 8, 9] conservative[10] and radical surgery,[11] and actual cautery,[12] but the protracted morbidity, the mutilating scarring, and the frequency of complicated sepsis or metastatic pus foci warrant the attempt of new method or methods to prevent these conditions.

Florey and Fleming[13] in their early work pointed out the fact that penicillin is more efficacious when used locally than when used systemically. This, coupled with Carp's[14] circuminjection of autogenous blood in the treatment of carbuncles, formed the basis of the early work on the method which we are about to describe. So far as we know, this method has not been used before.

During the past three years, we have used this method on many carbuncles. Our present series consists of 20 cases, all of which were large in size. Three of these patients were diabetics. The youngest patient was 11 years of age and the oldest 74, four were females, 16 males. The distribution of lesions is on the accompanying chart. Ten of the lesions were on the neck; four of the lesions were on the lips; three of the lesions were on the hands; one on the buttock; one on the thigh and one on the abdomen. This series of carbuncles was treated only by injection. No roentgen-ray nor incisions were used.

Carbuncle in the diabetic patients requires careful management and cooperation between the surgeon and internist. It is a well-established fact that infection renders the control of diabetes most refractory. McKittrick and Root[15] point out that the logical method of treatment demands immediate control of the patient's ketosis. Needless delay is often spent in futile attempts to control diabetes and limit the inflammatory processes by conservative methods. With the injection method no delay is encountered in limiting the inflammatory process, and the diabetes is more rapidly brought under control.

The method employed consists of the use of penicillin and novocaine. We used 100,000 units of penicillin per cc. of 2 per cent novocaine. There is no reaction between penicillin and novocaine, but the solution must be mixed just before using. On occasion the penicillin may precipitate. Five to 20 cc. of

* Submitted for publication, October, 1948.

this mixture is usually sufficient. The amount, of course, depends upon the size and distribution of the lesion. A very fine hypo needle (24 to 26 gauge) and a lock-type syringe have proved to be the best instruments for delivering the solution. The skin surrounding the carbuncle is carefully cleaned just beyond the indurated area. A small wheal is made in the skin. Considerable pressure is required for infiltration in this area. The needle is then carried into the deeper tissues where the solution may be injected with greater ease. The entire carbuncular area is surrounded. It is necessary to use from three to five points of injection. As the injection is given, one frequently sees necrotic

TABLE I.

Pt.	Age	Sex	Location of Lesion	Duration of Lesion	Size of Lesion	Number of Injections	Units Penicillin	Hospital Days	Days Lost	
HM	60	M	Neck	5 days	4 cm.	2	400,000	5	6	
JW	30	M	Neck	9 days	9 cm.	4	600,000	10	19	Diabetic
JC	47	M	Neck	2 days	6 cm.	2	400,000	4	10	
CB	28	F	Neck	5 days	6 cm.	2	400,000	0	5	
BW	11	M	Lower lip	5 days	3 cm.	1	500,000	4	9	
AJ	20	M	Neck	2 days	4 cm.	2	400,000	0	4	
WA	21	F	Hand	4 days	2 cm.	1	200,000	0	5	
MT	40	M	Buttock	7 days	10 cm.	5	1,000,000	10	25	Diabetic
AK	35	M	Lip	3 days	3 cm.	1	600,000	4	5	
LE	75	M	Neck	12 days	14 cm.	3	1,000,000	5	14	
MB	45	F	Thigh	8 days	14 cm.	3	1,000,000	4	10	
TH	50	M	Abdomen	7 days	6 cm.	2	500,000	0	3	
BH	45	M	Neck	5 days	8 cm.	2	750,000	0	7	
TS	30	M	Lip	3 days	4 cm.	3	1,000,000	7	14	Diabetic
MO	28	M	Hand	4 days	3 cm.	1	500,000	0	1	
TJ	34	M	Lip	2 days	3 cm.	1	1,000,000	4	4	
BR	60	M	Neck	7 days	12 cm.	4	1,500,000	3	8	
LW	35	M	Hand	4 days	5 cm.	1	300,000	0	2	
JM	30	M	Neck	5 days	8 cm.	1	1,000,000	5	10	
EB	56	M	Neck	7 days	8 cm.	2	1,600,000	0	2	

material exude from the center part of the lesion. Attention is called to the fact that the solution is not injected into the carbuncle, but around it, just beyond the indurated zone. Hot packs are recommended and the patient is seen daily. We have not found it necessary to anesthetize any of the patients in this series.

Figure 1 is a semi-diagrammatic explanation of the method employed.

The mode of spreading of a carbuncle is shown in Figure 2. The mode of spread also explains how the penicillin is able to attack the lesion directly. The column of Warren rests on the fascia. These structures are surrounded by a cell-like cuff, which just under the skin has a small defect, a festoon-like curve which connects the adjacent adipose column. It is through the openings below the skin, the adipose columns, and along the fascia that the infection spreads. By the same route the penicillin is able to reach the septic focus.

A typical course of a carbuncle of the neck treated in this manner is as follows: Immediately following the injection the patient is able to turn his

head, and frequently says, "This is the first time I have been free of pain in several days." He gets off the table without aid, and his entire expression has changed. Usually there is no tenderness at the site of injection. The carbuncle at this point shows pus exuding from the small openings. On the second day drainage is usually rather profuse. This drainage persists two or three days longer, depending upon the size of the lesion. A few of the openings coalesce, and healthy red granulation tissue is seen in the depths of the lesion. Epithelization is rapid. The resulting scar is thin and white, not adherent to the surrounding tissue. The induration subsides and is usually gone within two to four weeks.

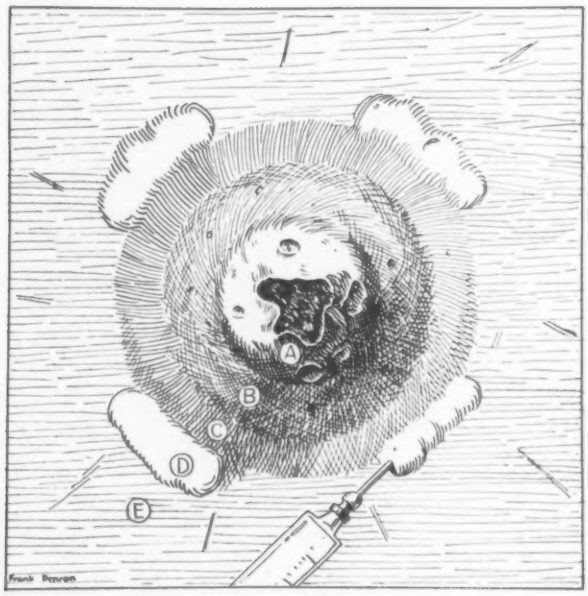

FIG. 1.—Semi-diagrammatic drawing of the various zones of a carbuncle.
A. Represents the necrotic and drainage area.
B. Slightly bluish and congested area.
C. The indurated area.
D. The wheal of penicillin and novocaine. At the completion of the injection, these wheals will be continuous. (After Kanavel)[16]

A Typical Case History: The last case listed on the chart reads as follows: E. B., on March 9, 1948, a 56-year-old farmer was referred to us complaining of a large carbuncle of seven days' duration on the neck. He had received no treatment whatsoever. The temperature was 99.6°; white blood count 18,600; 74% pmn. The urine was negative. The carbuncle measured 8 cm. in diameter. There were four draining sinuses and a small amount of pus present. Eight hundred thousand units of penicillin and 8 cc. of novocaine were injected into the area surrounding the carbuncle. Relief from pain was immediate. The patient was seen the next day, at which time the carbuncle was less painful. The patient stated that he had slept for the first time in a week. The carbuncle was draining profusely. Another injection of 800,000 units of penicillin and novocaine

was made in the area surrounding the carbuncle. The patient was seen the following day. The carbuncle was now soft, non-tender and not red. Drainage had all but disappeared. On March 16th, seven days after the first treatment, the carbuncle had healed. Epithelization was complete and there was a minimal amount of induration surrounding the original lesion. The patient stated that he had lost only two days of work.

By using this method, we have been able to shorten the morbidity of patients suffering from carbuncle. The tabulated chart shows the number of hospital days and the number of days actually lost from work. The average hospital stay in this series was three days. In spite of the size of the lesion

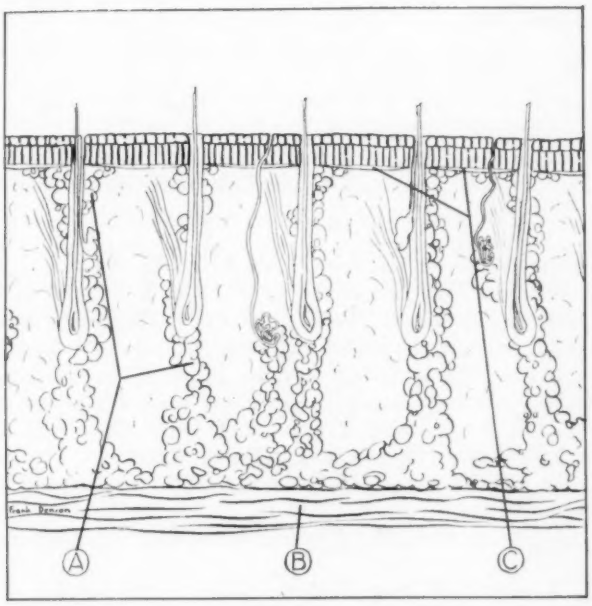

FIG. 2.—Semi-diagrammatic drawing of the gross section of skin and subcutaneous tissue.
A. The fat columns of Warren.
B. The fascia.
C. Festooning cuff at the top of the columns of Warren.

many of these patients were not hospitalized. In two instances the treatment was started at home. Otherwise the treatment was carried out as an office procedure. The average number of days lost in this series was 8.6. A great many of our patients returned to their jobs before epithelization was completed. They were able to do their own dressings, thereby cutting down the amount of time lost. There was no mortality in this series. This method may be employed at any stage of the disease, which is in contradistinction with the use of roentgen-ray in the treatment of carbuncles. After the time the slough begins to appear, roentgen ray is not efficacious. Surgical therapy is then often employed. None of the cases in our series failed to respond to the injection of penicillin, and no reaction to the treatment was encountered.

SUMMARY

1. A new method for the treatment of carbuncle has been presented. This may be used at any stage of the disease. The relief from pain is immediate. The method is simple and may be used as an office procedure.

2. A series of 20 cases treated in this manner with their results were given. There were no deaths in this series and no recurrence of the infection locally. The average hospitalization was three days and the time lost from work was 8.6.

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COMPLETE EXCISION OF PELVIC VISCERA IN THE MALE FOR ADVANCED CARCINOMA OF THE SIGMOID INVADING THE URINARY BLADDER*

ALEXANDER BRUNSCHWIG, M.D.

NEW YORK, N. Y.

FROM THE MEMORIAL HOSPITAL CENTER FOR CANCER AND ALLIED DISEASES
NEW YORK CITY

In a previous communication[1] a procedure was described for complete excision of the pelvic viscera for advanced carcinoma in the pelvis of the female in which there was involvement of uterus, bladder and rectum. The excretory functions of the alimentary and urinary tracts were provided for by an end sigmoid colostomy proximal to which there was bilateral implantation of the ureters (into the sigmoid). In the series of 22 instances reported, one of the cases listed was that of a male in whom a carcinoma of a redundant loop of sigmoid colon had infiltrated the urinary bladder beginning at the dome and extending downward toward the base. A segment of the lower ileum was also included in the carcinomatous mass. Because the situation in the male presents a number of problems different from that in the female, it is deemed justifiable to report the case in the male somewhat in detail since in the report cited above this patient was simply mentioned as an example of a successful case.

CASE HISTORY

M. P., male, age 46 years. Admitted to the private service of the writer at Memorial Hospital, January 2, 1948. In February, 1947, he had been seen in another institution where laparotomy had been performed for a carcinoma in the sigmoid colon. At this time a rather large carcinomatous mass in a redundant sigmoid was discovered to have attached itself to the dome of the urinary bladder. There were no liver metastases. There was no peritoneal spread but because of the attachment to the urinary bladder the situation was deemed inoperable. To relieve obstruction a double barreled colostomy was performed at about the junction of descending colon with sigmoid colon. Following this operation the colostomy functioned satisfactorily but there were severe cramping pains in the abdomen necessitating rehospitalization on three occasions. In general, the patient was unable to carry on his usual occupation. In the fall of 1947, the patient experienced several episodes characterized by severe chills and rise in temperature to 102° to 104°F. This resulted not only in discomfort at the time of the episode but there was marked general discomfort and feeling of disability for some days following the return of the temperature to normal.

Physical examination revealed a rather emaciated male of stated age. The patient seemed rather nervous and very easily upset emotionally.

General physical examination of the abdomen revealed no evidences of ascites, periumbilical cutaneous metastases or enlarged inguinal nodes. The double barreled colostomy in the left lower quadrant was satisfactory. The muscles of the abdominal wall seemed to be held rather rigidly although there was no pain on superficial or deep palpation. The liver was not palpable. Rectal examination revealed at the tip of the examining finger a firm, rather fixed mass which could not be directly palpated within the lumen of the pelvic colon. This mass seemed fixed to the bladder anteriorly and could not be moved easily in relation to the sacrum. No discreet nodules were palpated in the cul-de-sac.

* Submitted for publication, October, 1948.

Laboratory examinations were as follows: Plasma proteins 6.9 Gm.%; B. U. N. 8.9 mg.%; W. B. C. 8,800; Hemoglobin 13. Gm.; Urinalysis albumin 4+; sugar 0; many leukocytes. Roentgenographic study of chest: No evidence of pulmonary metastases.

Operation (Figs. 1A and 1B) January 10, 1948. Ether anesthesia (with curare).

Assistants: Drs. T. Walsh and H. J. VandenBerg.

A low midline incision was made to enter the abdomen. There was no free fluid nor immediate evidence of peritoneal metastases. The liver was palpated and inspected and was free from metastases. The spleen was not enlarged. Several large, soft, peri-aortic nodes were palpated and one at about the level of the umbilicus was excised and sent for frozen section diagnosis. The report was returned as showing no evidence of metastatic carcinoma.

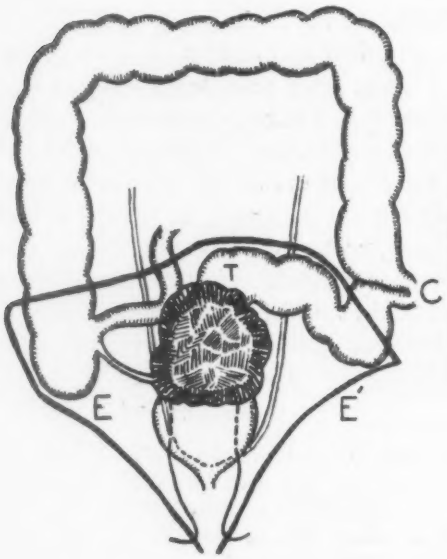

FIG. 1.—A. Diagram showing T, carcinoma arising in redundant loop of sigmoid that has invaded dome of urinary bladder, tip of appendix and loop of ileum. C, double barrel colostomy performed a year previously. Lines E, E', indicate extent of operation. (See Text.)

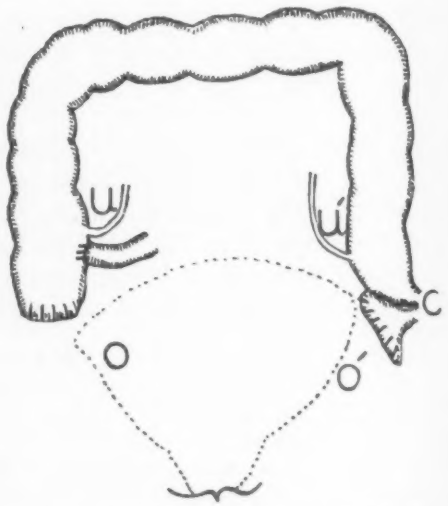

FIG. 1.—B. Diagram illustrating postoperative condition. U, right ureter implanted into ascending colon above ileocolostomy. U', left ureter implanted into lowest segment of descending colon above colostomy, C, O, O', area denuded of peritoneum after excisions described.

In the lower abdomen a large rounded mass, obviously a carcinoma, surrounded by considerable inflammatory reaction was found. Coursing into the upper portion of this mass the loop of sigmoid colon below the double barreled colostomy could be traced but in the mass it seemed to lose its identity. A segment of lower ileum about 10 cm. in length also was attached to the mass on its upper right aspect. Palpating inferiorly the mass seemed to be continuous with the dome of the urinary bladder. Palpation downward into the true pelvis on each side of the mass and bladder revealed no infiltration between the mass and bladder on the one hand and the sides of the pelvis. It also was noted that the appendix seemed to be pulled into the mass and was stretched rather tightly.

While the mass was being palpated and moved from one side to another to determine any extensions into posterior abdominal wall or lateral pelvic walls, a separation was made on its superior surface with escape of about 30 cc. of thick, yellow pus with typical fecal odor. It became obvious that in the center of the mass there was an abscess that had

been inadvertently opened. The pus was sponged away as quickly as possible and gauze plugs were placed into the tear.

Both hypogastric arteries and veins were isolated, doubly ligated and transected. Arterial and venous branches coursing downward and forward toward the bladder and the lower pelvic colon were likewise isolated, ligated and divided. The peritoneum at the level of the pelvic brim was incised and by digital and gauze dissection it was elevated toward the midline all the way around. The peritoneum reflecting from the anterior abdominal wall onto the anterior aspect of the bladder was incised and by means of gauze

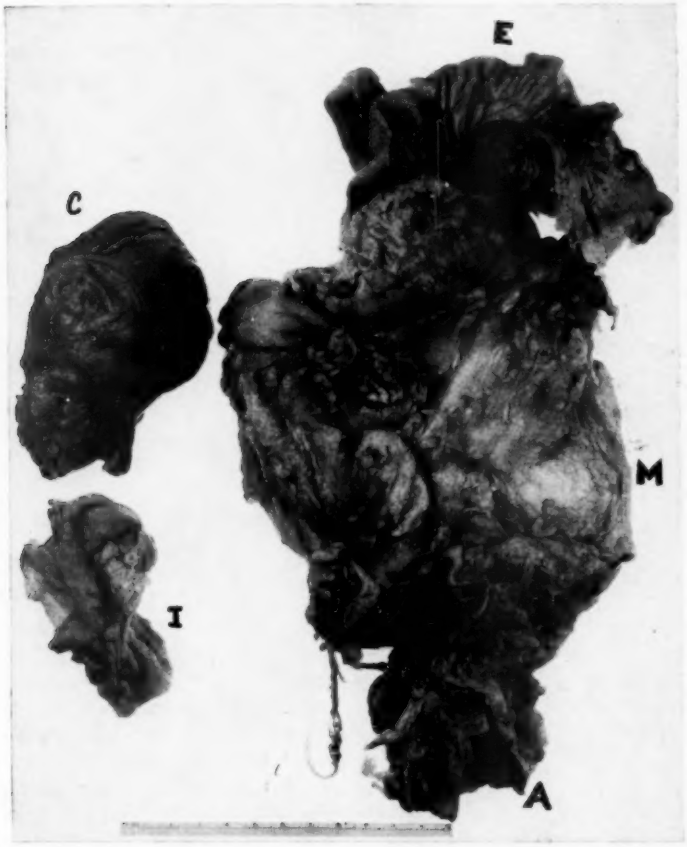

FIG. 2.—Photograph of surgical specimens. M, large neoplastic mass including pelvic and sigmoid colon, urinary bladder (and lower ureters and prostate). E, segment of lower ileum invaded by neoplasm. A, anus. C, caecum and lower ascending colon. I, small segment of ileum just proximal to caecum.

and digital dissection the mass and bladder were freed from the inner surfaces of the symphysis pubis and adjacent portions of the bony pelvis. Continuation of this dissection all the way around including the hollow of the sacrum resulted in mobilization of the mass which consisted of tumor, lower sigmoid and pelvic colon and urinary bladder from the sides of the pelvis in all directions. The only attachments remaining were superiorly with the sigmoid and ileum and inferiorly on the urogenital diaphragm.

The sigmoid colon, about 6 cm. below the double-barreled colostomy, was transected and each end invaginated by purse string suture. This resulted in a small segment of sigmoid remaining as the lower limb of the double-barreled colostomy in the left lower quadrant. The mesosigmoid was transected at its origin and the large vessels secured and

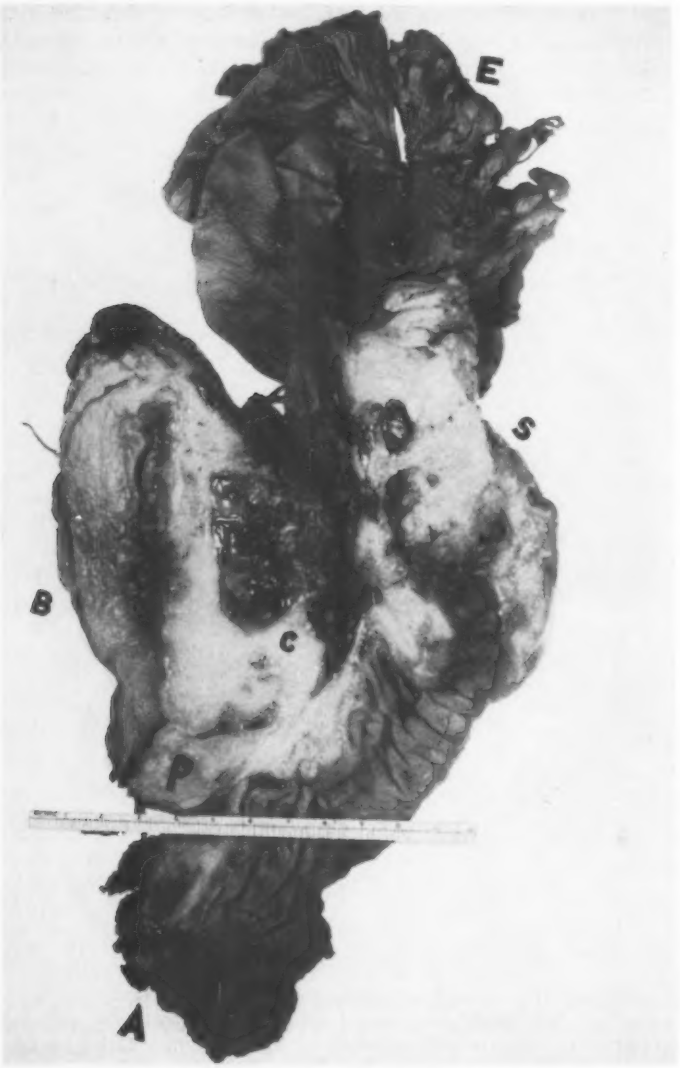

FIG. 3.—Mass M, shown in Fig. 2, has been bisected. E, segment of lower ileum. S, sigmoid and site of primary growth. B, urinary bladder, P, prostate. C, neoplasm with necrotic center (abscess). Extensive invasion of posterior bladder wall is shown. A, anus.

ligated. Mobilization of the lower ileum and cecum was then begun by elevation from the posterior abdominal wall. The segment of ileum involved in the mass was isolated and divided between clamps. In isolating a triangular portion of mesentery corresponding to this segment of ileum, large vessels going to the cecum were transected and ligated. In

a few moments the cecum became somewhat cyanotic and it was deemed necessary to excise this also. The cecum and lower half of ascending colon were then completely mobilized and the ascending colon transected in its mid portion, the upper segment being invaginated by a triple row of sutures. The ileum was then anastomosed to the ascending colon end-to-side.

Both ureters could now be well inspected and were found not dilated nor involved by neoplasm above the pelvic brim. The ureters were transected at about the level of the fourth lumbar vertebra. The right ureter was implanted into the upper portion of ascending colon by means of a modified Coffey I. technique. The left ureter was implanted into the descending colon about 6 cm. above the colostomy also by a modified Coffey I. technique. The abdominal wound was then closed in layers with soft rubber drains in the inferior angle of the wound.

The patient was then placed in lithotomy position and an elliptical incision made about the anus after the latter was closed with purse string suture. It extended forward on the right side of the base of the scrotum a little farther than would ordinarily be the case in the usual combined abdomino-perineal resection. The levator ani muscles were divided and the anal colon completely mobilized.

Dissecting with scissors the lower portions of the pelvic colon were then liberated first on the right and then on the left side by division of musculo-fascial attachments of the pelvic floor.

The urethra was transected as it emerged from the inferior portion of the prostate. The inferior and lateral attachments of the latter were divided completely.

The bladder, prostate, anal, pelvic and sigmoid colons with tumor mass and attached segments of ileum were removed through the pelvic floor.

The defect in the pelvic floor was closed by interrupted catgut sutures for the muscles and fascia and a separate layer of catgut sutures for the skin and subcutaneous fat. A hard rubber tube drain was inserted through the repaired pelvic floor to drain the lower true pelvis.

Duration of operation: Five hours.

Fluids administered intravenously: 5000 cc. blood; 1500 cc. plasma; 1500 cc. normal saline; 500 cc. 5% dextrose.

Gross pathologic study: See accompanying Figs. 2 and 3.

Histologic diagnosis: Adenocarcinoma of colon with invasion of bladder, ileum and metastases to lymph nodes in meso-sigmoid.

The postoperative course was prolonged and complicated by the development of deep pelvic abscess and abscesses in the abdominal wall. However, urinary and fecal drainage from the colostomy was satisfactory from the day after operation. Intravenous pyelograms taken on the 19th day after operation showed moderate bilateral hydronephrosis.

On the third day after operation the B. U. N. was 40.3 mg. % and thereafter progressively fell to 15.1 mg. % on the day he was discharged. The patient left the hospital on the 39th day after operation, ambulatory, free from abdominal pain and with no fever. Since discharge he has gained 25 lbs in weight.

At this writing, one year and two months after operation, he is returned to his usual occupation, that of a merchant, and wears a Rutzen bag over the colostomy (sealed to the skin). Physical activities are essentially normal. He is without pain, and has taken business and pleasure trips.

DISCUSSION

The successful outcome of the operation with return to his usual occupation and relief from pain and episodes of chills and fever of urinary tract origin, illustrates again the palliation that is sometimes possible in the face of desperate situations that may be encountered at the time of laparotomy. One year prior to the operation described, this patient presented the criteria of advanced and

"inoperable" carcinoma. The case record also illustrates again how certain abdominal neoplasms (of the colon in this instance) may progress locally to a marked degree before liver metastases may become manifested. Finally, the feasibility of complete excision of pelvic viscera in the male has been demonstrated as a counterpart of the procedure devised for advanced pelvic cancer in the female.

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ADAMANTINOMA OF THE MANDIBLE*

A CASE REPORT

DANIEL CATLIN, M.D.

NEW YORK CITY

FROM THE MEMORIAL HOSPITAL, NEW YORK CITY

AN ADAMANTINOMA is a rare epithelial tumor arising from the enamel organ either in the mandible or maxilla. This slowly growing tumor is locally malignant (similar to a basal cell epithelioma of the skin) and on rare occasions has been noted to metastasize. A review of the medical records of the Memorial Hospital for the 21-year period 1927 through 1947 reveals that 51 patients received treatment for adamantinomata; in each case the clinical diagnosis was confirmed by histopathologic examination of the tumor tissue. The disease was found in 27 males and 24 females. The mandible was the site of origin of the tumor in 42 cases and the maxilla in nine cases. Two of the adamantinomata metastasized; one to a regional lymph node, the other systemically to the lungs resulting in death to the patient.

A detailed discussion of adamantinoma (its clinical characteristics, histopathology, treatment, and review of the literature) is not the intent of this report. It is sufficient to state that our treatment of this tumor during the past 10 years or more has been by radical surgical removal. In the lower jaw, partial resection of the mandible is usually required. In the upper jaw, removal of one maxilla (sparing the floor of the orbit) is the procedure of choice.

The purpose of this paper is to report the surgical management of one patient with a very extensive adamantinoma of the mandible. The case is of unusual interest for two reasons: (1) the tumor was of sufficient size to require resection of the entire mandible in one stage. (2) There was a solitary metastasis to a regional lymph node.

CASE REPORT

J. C., a 32-year-old Negro, came to the Memorial Hospital on Dec. 21, 1946, complaining of a "lump" in the jaw of 6 years duration. Being a part-time professional boxer, the patient naturally (and erroneously) believed his tumor was caused by a punch on the jaw. Four years ago, a partial removal of the tumor was attempted through a submental approach. Following this operation the tumor continued to grow. The patient stated his general health was excellent.

Examination: A well developed, healthy appearing Negro, with a huge 15 cm. bony tumor of the mandible extending from the second molar tooth on the right to the second bicuspid tooth on the left (Fig. 1). The overlying skin was freely movable; two areas of superficial ulceration were noted in the mucosa of the right lower gingiva. The most unusual finding was a 4 cm., rubbery, freely movable, left posterior submaxillary lymph node (Fig. 2).

Clinical Diagnosis: Adamantinoma of mandible, with possible metastasis to left submaxillary lymph node.

* Submitted for publication, December, 1948.

Laboratory Data: Biopsy of tumor of mandible: Adamantinoma. Aspiration biopsy of left submaxillary lymph node: Metastatic adamantinoma. Roentgen-ray film of chest: Essentially normal.

Blood: Mazzini: Negative for syphilis.

Submitted roentgen-ray film report of mandible: "Multicystic process involving a great deal of the mandible on both sides of the symphysis."

The patient was admitted to the hospital on January 14, 1947. On January 17th a total mandibulectomy and bilateral submaxillary neck dissection was performed.

Operative Procedure: A preliminary tracheotomy was made under local 2% Monocaine anesthesia. The patient was then anesthetized with intravenous pentothal (2.5% solution), oxygen being supplied by a closed respiratory system through the tracheostomy

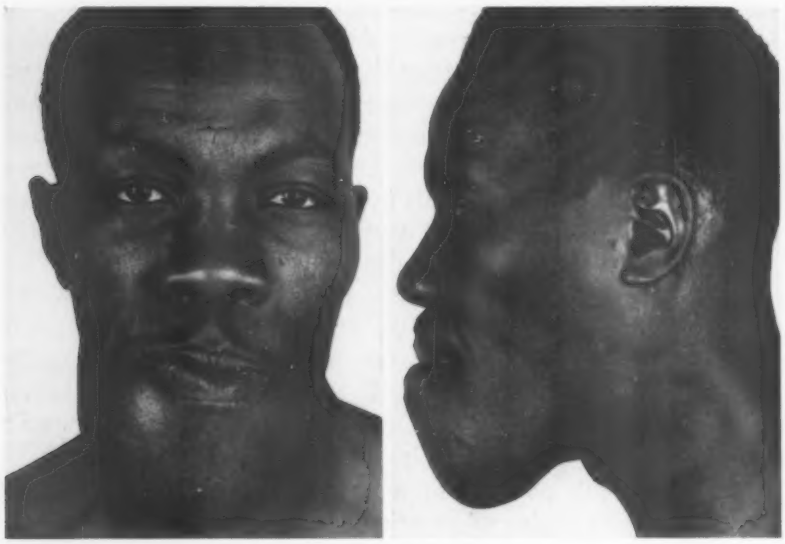

FIG. 1 FIG. 2

FIG. 1.—Full face preoperative appearance (December, 1946).

FIG. 2.—Left lateral preoperative appearance (December, 1946) showing metastatic node in left upper neck.

tube. The lower lip was split with two vertical incisions 2.5 cm. apart, each incision being carried posteriorly across the submaxillary triangle to the anterior margin of the sternocleidomastoid muscle on each side (Fig. 3). Flaps composed of skin, subcutaneous fat, and platysma muscle were then developed and reflected laterally, exposing both submaxillary triangles (Fig. 4). An enlarged lymph node was noted in the left posterior submaxillary area. The external carotid arteries were identified on both sides and were ligated with steel wire just distal to their superior thyroid branches. Both submaxillary triangles were then cleaned out including the submaxillary glands; the soft tissue of this dissection remained attached to the mandible superiorly.

The hypopharynx was packed with gauze and the operative incision carried into the mucosa of the oral cavity around the tumor (Figs. 5 and 6). The right mandible was disarticulated by dividing the masseter, pterygoid and temporal muscles and finally the capsule of the temporomandibular joint. The muscles in the floor of the mouth were severed from the mandible. The left mandible was disarticulated in a manner similar to

FIG. 3.—Skin incision showing removal of a central segment of lower lip. Note tracheostomy tube in place.

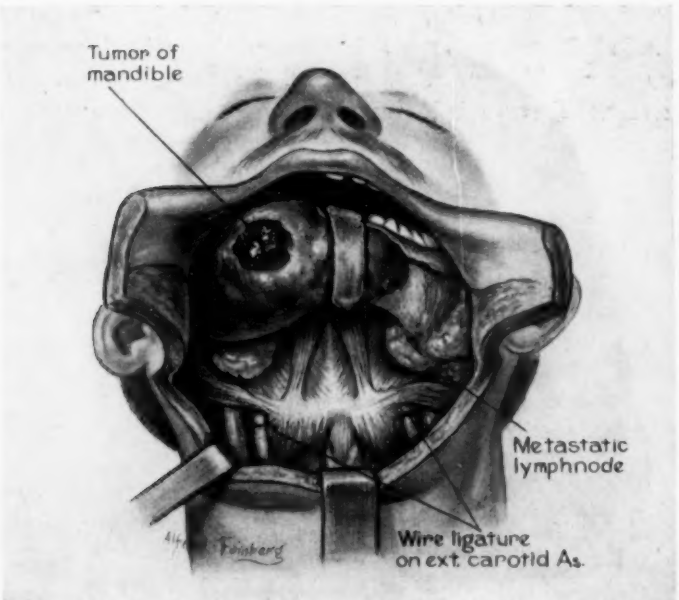

FIG. 4.—Skin flaps retracted revealing tumor of mandible and metastatic node in left neck.

the right side.* The operative specimen consisting of the entire mandible and the contents of both submaxillary triangles was removed en masse (Fig. 7).

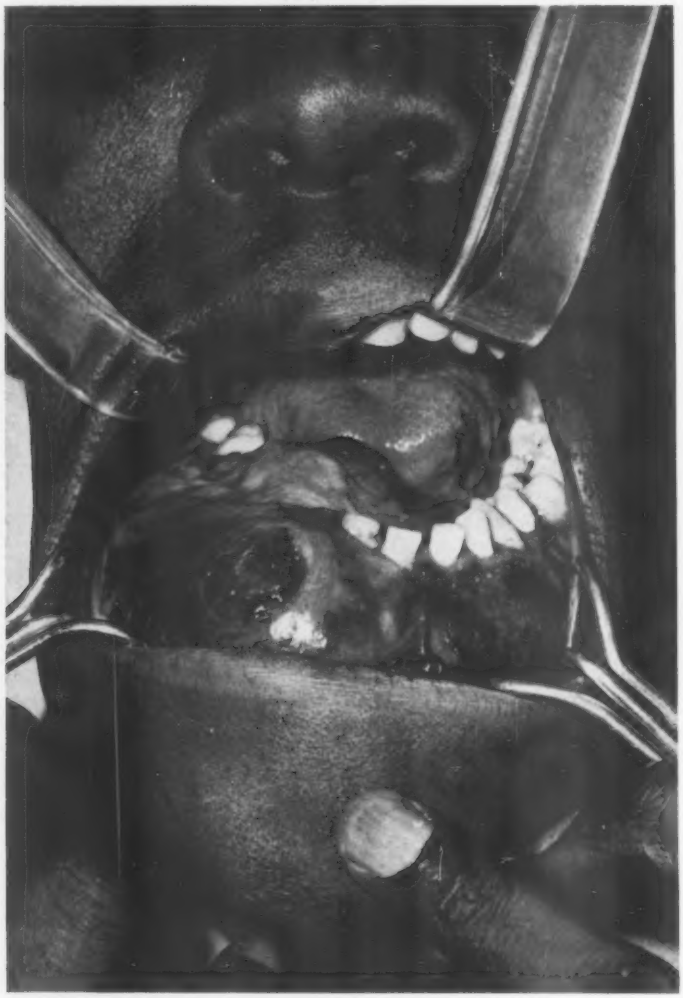

FIG. 5.—Intra-oral appearance of tumor.

* When a major portion of the mandible must be resected and immediate plastic reconstruction of the bony defect is not desirable, experience has shown us that disarticulation at the temporomandibular joint is preferable to leaving a portion of the ascending ramus in place. Any remaining fragment of the mandible is displaced upward by the pull of the temporal muscle and medially by the action of the internal pterygoid muscles. In such a position the ascending ramus is useless for mastication while its medial displacement into the oral cavity often causes some interference with the normal act of deglutition. This disadvantage can be eliminated by disarticulation of the mandible.

The complete removal of a malignant tumor of the mandible is of much greater importance to the ultimate prognosis than a fine cosmetic end result. Therefore, we seldom attempt an immediate plastic repair of the operative defect.

FIG. 7.—Operative specimen.

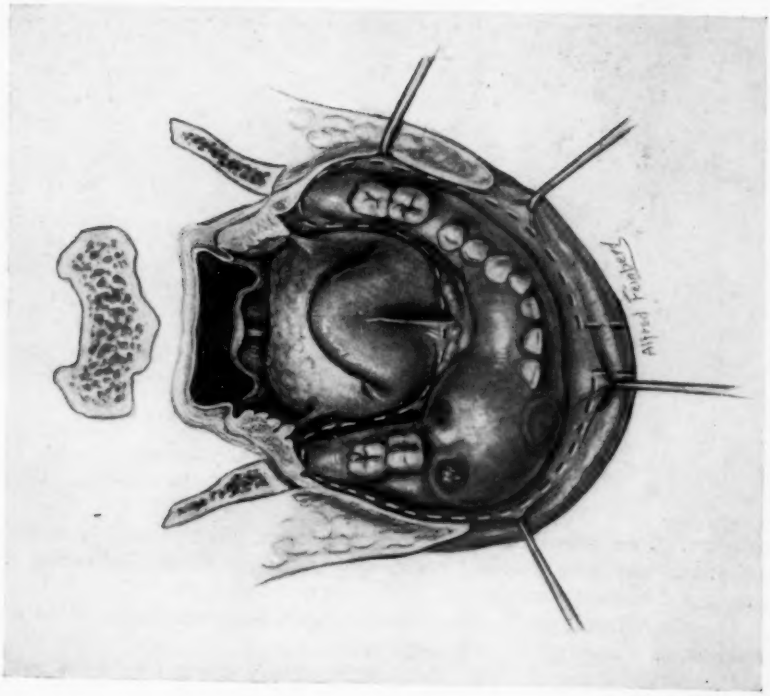

FIG. 6.—Intra-oral operative incision.

The external and intra-oral operative incisions were carefully closed with interrupted vertical mattress sutures of Dermalon; a rubber tube drain was placed in each pterygoid fossa (Fig. 8). A pressure dressing was applied. The operating time was 4 hours. The patient received 1,500 cc. of whole blood and 500 cc. of 5% dextrose solution during the

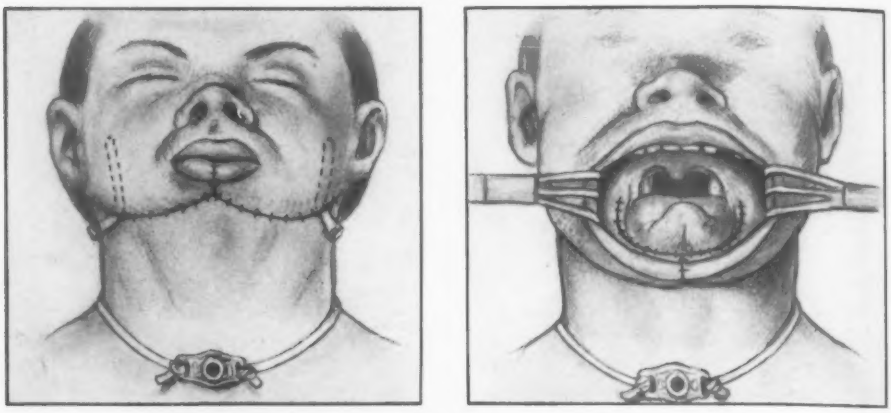

FIG. 8.—External and intra-oral suture lines.

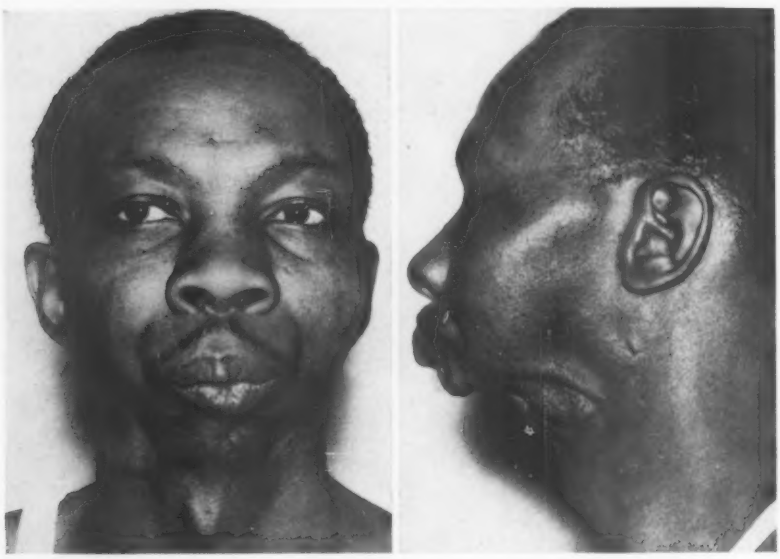

FIG. 9 FIG. 10

FIG. 9.—Full face postoperative appearance. (December, 1948).
FIG. 10.—Left lateral postoperative appearance. (December, 1948).

procedure. Two grams of sodium pentothal were administered. The blood pressure, respirations, and pulse remained steady during the operation. The patient was returned to the ward in good condition.

Pathologic report on the operative specimen was adamantinoma of the mandible with metastasis to a solitary cervical lymph node.

Postoperative course. The postoperative recovery was uneventful and satisfactory. Penicillin (50,000 units every three hours) was given intramuscularly for five days

following which the temperature remained normal. Two 500 cc. blood transfusions were given, the first on the fourth and the second on the sixth postoperative day. High caloric, high vitamin, liquid feedings were started on the first postoperative day; the formula was given through a No. 16 urethral catheter which was passed through the nasal cavity into the cervical esophagus. The oral cavity was thoroughly cleaned with a power spray of saline solution twice a day; a gauze pack saturated with a thin solution of zinc peroxide was maintained in the oral cavity along the suture line.

The drains were removed from the pterygoid fossae on the 3rd postoperative day. The tracheostomy tube was corked on the 4th day and removed on the 5th.

The patient started drinking a liquid diet by mouth on the 5th day and was discharged from the hospital on the 10th day. The external and intra-oral wounds were healing by primary union; all skin sutures were removed. However, the patient was partially incontinent of saliva which drooled from his unsupported and edematous lower lip.

During the subsequent five days all sutures were removed from the oral cavity wound, the edema of the lower lip subsided, and the patient ceased to drool. His speech became distinct and he was able to eat a soft diet.

This patient has been examined at regular intervals in our Recall Clinic. His general health remains excellent and there is no further evidence of recurrent or residual tumor. At the time of his last examination on December 15, 1948, he had returned to his regular job as a porter and is self-supporting.

SUMMARY

The surgical management of a 32-year-old Negro with a huge adamantinoma of the mandible and with a metastatic cervical lymph node is discussed. Pictures of the patient and drawings of the operation are presented.

SPONTANEOUS RUPTURE OF THE ESOPHAGUS*

JOHN M. BEAL, JR., M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY OF THE NEW YORK HOSPITAL AND CORNELL UNIVERSITY MEDICAL COLLEGE

SPONTANEOUS RUPTURE of the esophagus is sufficiently uncommon to justify the reporting of this case. The frequent difficulty in diagnosis is illustrated by this case and emphasizes the importance of early diagnosis if recovery is to be made in this condition which has had a mortality rate approaching 100 per cent.

CASE REPORT

H. G., N. Y. H. No. 166320, a 52-year-old white married laborer, was admitted to the New York Hospital for the first time on May 26, 1948, complaining of left chest pain and shortness of breath. The night prior to admission, the patient had consumed an unknown quantity of beer and had retired at midnight. At 4.20 A.M. he awoke with the desire to defecate and, while straining at stool, he suddenly became nauseated and vomited. The character of the vomitus was not noted. He had the sudden sensation of "something giving way, the stomach went up and never came down"; associated with this was a severe pain in his epigastrium and left lower chest and he experienced marked shortness of breath.

Past History. Pneumonia at age of 15; "pleurisy" in 1934, following a "cold," without sequelae; in 1944 a chest plate revealed a nodular tuberculous infiltration at the second left interspace apparently stable and repeat chest x-ray two months later revealed no change in this lesion. Patient consumed four or five glasses of beer daily.

Review of system: Chronic nasal discharge and chronic non-productive morning cough; epigastric distress and "gas" following meals, relieved by alkali for about one year.

Physical Examination. T 37° C; P 130; R 22; BP 180/120. On admission at 5A.M. the patient was well developed, moderately obese and in acute distress, slightly cyanotic with grunting respirations. Lungs: Slight dullness at left base but otherwise clear; Abdomen: distended and tympanitic with resistance and tenderness high in the left upper quadrant.

Laboratory. Sp. gr. 1025; reaction acid; albumin 4 plus; sugar 0; occasional RBC and WBC in sediment. Blood: HGB 17 Gm.; RBC 7.2 million; WBC 14,800 with 72% polymorphonuclear leucocytes.

A plain film of the abdomen was negative and a chest film revealed the posterior half of the diaphragm to be covered by a layer of fluid on the lateral projection.

Three hours following admission the patient's blood pressure had fallen to 130/110 and the pain became more localized to the left lower chest. A tube was passed into the stomach without difficulty and 1000 cc. of fluid and a moderate amount of air was aspirated. A thoracentesis was performed in the left eighth interspace and 850 cc. of brownish fluid obtained. Three hundred thousand units of penicillin was introduced into the pleural cavity at this time. The pleural fluid was found to contain 121,000 WBC/mm^3 and 5,000 RBC/cmm. A chest plate taken after completion of this procedure disclosed bilateral pleural effusion. Not reported at this time but noted later in reviewing the film was the presence of minimal mediastinal and cervical subcutaneous emphysema. An EKG showed sinus tachycardia and left axis deviation.

* Submitted for publication, October, 1948.

The patient was placed in an oxygen tent and parenteral fluids and large doses of penicillin were administered. His pulse varied from 100 to 140, and his course was febrile, fluctuating from 38. to 38.6° C rectally.

On May 28, 1948, thoracentesis was again performed and 200 cc. of dark brown fluid was withdrawn, 300,000 units of penicillin and 0.5 Gm. of streptomycin were instilled into the pleural space. The patient was also started on intramuscular streptomycin. Culture of the pleural fluid yielded gamma non-hemolytic streptococci, *B. proteus vulgaris, Cl. welchii* and *E. coli*. The patient took oral fluids in adequate amounts after the third hospital day. He continued to be cyanotic when out of the oxygen tent and appeared acutely ill. Daily thoracentesis was performed with instillation of penicillin and streptomycin. By June 2nd, 1948, cultures of the pleural fluid were overgrown with *Monilia albicans* and roentgenograms of the chest revealed locculated fluid in the left chest with pockets of air.

On June 3, 1948, open drainage of the empyema cavity was performed under local anesthesia, supplemented with sodium pentothal. A large empyema cavity was found, the walls of which were covered with a grayish-green fibrinous slough and communicated with the posterior mediastinum. Drainage was instituted with 6 cigarette drains and 2 soft rubber tubes. Postoperatively streptomycin and penicillin were continued but the patient's course was progressively downhill, with elevation of pulse and temperature. The patient expired on the fifth postoperative day, 13 days after entering the hospital.

At autopsy, a perforation two and a half centimeters in diameter in the posterior portion of the terminal esophagus was found, just above the diaphragm. There was no evidence of ulceration or tumor. The perforation communicated with the posterior mediastinum and left pleural cavity. There was posterior mediastinitis and a left empyema with surgical drainage. The pericardial sac contained 50 cc. of cloudy fluid and there was thickening of the visceral and parietal pericardium. Additional findings were those of a chronic gastric ulcer on the lesser curvature 6 cm. from the pylorus and a second small acute ulcer in the pylorus. There was bilateral chronic pyelonephritis with minimal hydronephrosis. A calcified tuberculous nodule was found in the left upper lobe.

DISCUSSION

The majority of references to spontaneous rupture of the esophagus in the literature are in the form of case reports. According to Eliason and Welty[4] the first recorded case was that described by the Dutch physician Boerhaave in 1724. Extensive reviews of the subject have been made by Fitz[5] in 1877, Walker[13] in 1914 and Klein and Grossman[9] in 1943, the last named authors being able to find 40 cases in the literature to that date.

Recovery has seldom been recorded, and most authors consider the condition uniformly fatal (Frink,[6] Eliason and Welty[4]); however, survival has occurred in three instances when drainage of the resulting empyema was followed by recovery. Ballin and Salzstein[1] in 1922 described the case of a 15-year-old boy who developed empyema following an episode of severe vomiting. The boy recovered after drainage of the empyema cavity although an esophageal fistula persisted for approximately a year after operation. In an editorial comment in 1944, Graham[7] stated that he had seen two cases in which drainage of the empyema cavity resulted in healing. Direct attack on the defect in the esophagus has seldom been attempted, largely due to the difficulty in making the diagnosis early enough. In 1944 suture of the esophagus following spontaneous rupture was carried out by Collis;[3] however, the patient survived only 21 hours after operation. Hertzog and Leighton[8] in 1946 performed closure

of the esophagus with drainage. The patient expired on the sixth postoperative day from a pulmonary embolus. The first successful closure was reported by Barrett[2] in 1947. He records the case of a 46-year-old female who developed an episode of sudden vomiting (13 days after hysterectomy) resulting in rupture of the esophagus. Operation was performed 10 hours after perforation; closure was accomplished and drainage instituted with satisfactory recovery.

Although this catastrophe usually occurs in adults after the third decade of life, it has been recorded in childhood. Menne and Moore[11] in 1921 submitted the case of a five months old female and cited three others in children aged 4 months, 3 years and 7 years.

ETIOLOGY

An adequate explanation of rupture of the apparently healthy esophagus is still lacking. The earliest investigations were those of Zenker and von Ziemssen[15] and of McKenzie.[10] These workers demonstrated the lower portion of the esophagus was the weakest when distended by water and that pressures of from 5 to 11 lbs. of water were required to cause rupture of the esophagus. Weiss and Mallory[14] studied lesions about the cardiac orifice of the stomach produced by vomiting and at autopsy found fissure-like lesions in the mucosa in patients who had been vomiting persistently. In their analysis, they concluded "that pressure changes in the stomach during the disturbed mechanism of the coordinated motor changes which accompany vomiting and continual regurgitation of gastric juice over the mucosa of the cardia are the most significant changes."

Anatomically, the esophagus is a vertical midline organ; however, in its upper portion it extends slightly to the left of the midline, in the lower portion deviates somewhat to the right and then veers to the left to pass through the esophageal hiatus to join the stomach. The act of vomiting is initiated by a rapid inspiration and closure of the glottis. The pyloric portion of the stomach constricts and the contents of the stomach are forcibly ejected through the relaxed cardiac orifice by contraction of the abdominal wall musculature. Thus, gastric contents are forced suddenly against the weakest portion of the esophagus with considerable force. The investigations of Weiss and Mallory[14] show that fissures in the mucosa about the cardiac orifice are frequently produced without rupture occurring. Vinson[12] reported cases of stricture of the lower esophagus following the pernicious vomiting of pregnancy. The findings indicate that frequently vomiting may produce tears in the mucosa of the esophagus but not involving all layers, and suggests that rupture may occur "spontaneously" in an esophagus that is already weakened by fissures from previous episodes of vomiting.

CLINICAL PICTURE

The patient is usually a middle-aged male from whom a history of frequent intake of alcohol is obtained. The episode usually occurs after ingestion of a quantity of intoxicating drink or a heavy meal. Vomiting is followed by the sudden onset of high epigastric and left lower chest pain and the patient may describe the sensation of tearing associated with the act of vomiting.

On examination the patient appears acutely ill and presents a rapid pulse and lowered blood pressure. Dyspnea is usually present associated with splinting of the chest and grunting respiration. Because rupture of the esophagus is usually followed by the extravasation of gastric contents into the left pleural cavity, signs of a left pleural effusion may rapidly develop. Tenderness in the epigastrium or left upper quadrant are present.

Roentgenograms of the chest show pleural effusion early and this finding is progressive. Significant is the finding of mediastinal emphysema which is easily overlooked. If thoracentesis is performed, the aspirated fluid should be titrated for free acid. Some patients have been given barium by mouth and the defect in the esophagus demonstrated by the extravasation of the barium into the pleural cavity.

TREATMENT

The recent cases of Hertzog[8] and of Barrett[2] indicate the importance of early diagnosis with the view of undertaking prompt operation to accomplish closure of the defect. Early measures are thus to be directed toward establishing the diagnosis and preparing the patient for operation. Accordingly, oxygen, sedation, antibiotics and hydration are indicated. There is some question as to whether or not a tube should be passed into the stomach. It would seem that an attempt should be made for if the tube were to enter the pleural space, it would aid in establishing conclusively the diagnosis; however, if the tube were to be passed successfully into the stomach, not only would it aid in decompressing the stomach and help prevent further insult to the pleural cavity by the acid gastric content, but technically it might facilitate the operative procedure by allowing more ready identification of the esophagus at the time of thoracotomy.

At operation Barrett[2] advises transpleural closure of the defect followed by closed underwater drainage of the pleural space. Cultures of the pleural fluid should aid in the choice of antimicrobial therapy.

SUMMARY AND CONCLUSIONS

A case of spontaneous rupture of the esophagus is presented.

The etiology of the condition is discussed. Investigations and clinical findings suggest that it is the result of direct force of the gastric contents in vomiting upon an esophagus that may have undergone pathologic changes.

Early diagnosis and operation should provide for recovery in this formerly uniformly fatal condition.

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CONGENITAL INTESTINAL ATRESIA*

EDWARD E. JEMERIN, M.D. AND CYRILLE R. HALKIN, M.D.
NEW YORK, N. Y.

CONGENITAL INTESTINAL ATRESIA is an uncommon condition although the true incidence is probably considerably higher than that indicated by the number of cases which have reached the literature. Most cases have not been recorded until recently, and even now many infant deaths due to intestinal atresia remain undiagnosed or are not reported. Until some central Registry for the recording of such cases is set up, it is incumbent upon any physician encountering one to see that at least a brief report is entered in the literature. This is particularly the case in view of the extremely high mortality associated with the malformation, a mortality which early recognition and prompt adequate treatment seems to be lessening appreciably. The case encountered by the authors was that of a complete high jejunal atresia in a three and one-half pound premature infant who recovered following jejuno-jejunostomy, the smallest case on record in which a successful result was achieved. An incomplete rotation of the colon was also present but this was not obstructing and did not therefore influence the clinical picture or appreciably alter the surgical problem.

CASE REPORT

F. G., Sydenham Hospital No. 108318, was a premature male infant spontaneously delivered on March 12, 1948, after a 30-week gestation (Dr. Daniel Wanderman). There had been two previous pregnancies; a full term stillbirth four years before, and a full term forceps delivery of a normal boy two years ago. The mother was Rh negative with no demonstrable antibody formation. No history of virus infection during pregnancy could be elicited.

The infant weighed 3 lbs. 14 ozs. at birth and was cyanotic but responded to aspiration and oxygen. Physical examination revealed marked overriding of all skull bones at the parietal, sagittal and occipital sutures, with complete closure of the anterior and posterior fontanelles. The eyes were wideset and a cataract-like lesion of the right was noted. The lungs were fully aerated, the heart normal. The abdomen was soft, the liver edge palpable one finger below the costal margin.

The infant was placed in an incubator with continuous oxygen and 5 mg. vitamin K daily. Pediatric care was supervised by Dr. Lawrence B. Slobody. After twelve hours of starvation, small amounts of glucose water were offered for twelve hours followed by a 1:3 evaporated milk formula. On the second day after delivery, regurgitation after feeding began, the milk curds being mixed with thin yellow fluid. Moderate icterus and a petechial rash on the bregma and the dorsum of the feet were noted, and the temperature rose to 102.8 degrees. A small meconium stool was passed. All oral feeding was stopped and intensive parenteral hydration with saline and Hartman's solution was begun. Intramuscular penicillin was also given. Intermittent vomiting continued and by the evening of the third day, the infant appeared markedly dehydrated and in very grave condition. There was no appreciable distention and no peristaltic waves or pyloric tumor were observed.

* Submitted for publication, December, 1948.

On the fourth day, the general condition was somewhat better. The icterus had deepened but the state of hydration had improved. Regurgitation continued but the infant seemed to retain small amounts of gavage feedings which had been added to the regimen. Several more meconium stools were passed. The blood count revealed a hemoglobin of 14.5 Gm., a red blood count of 5,020,000 per cu. mm., and a white blood count of 24,600 per cu. mm. with 16 immature forms, 57 mature polymorphonuclear leucocytes, 1 eosinophil, 22 lymphocytes, 4 monocytes and 1 nucleated red blood cell per 100 whites. A slight trace of bile was present in the urine. A plain roentgen film of the abdomen

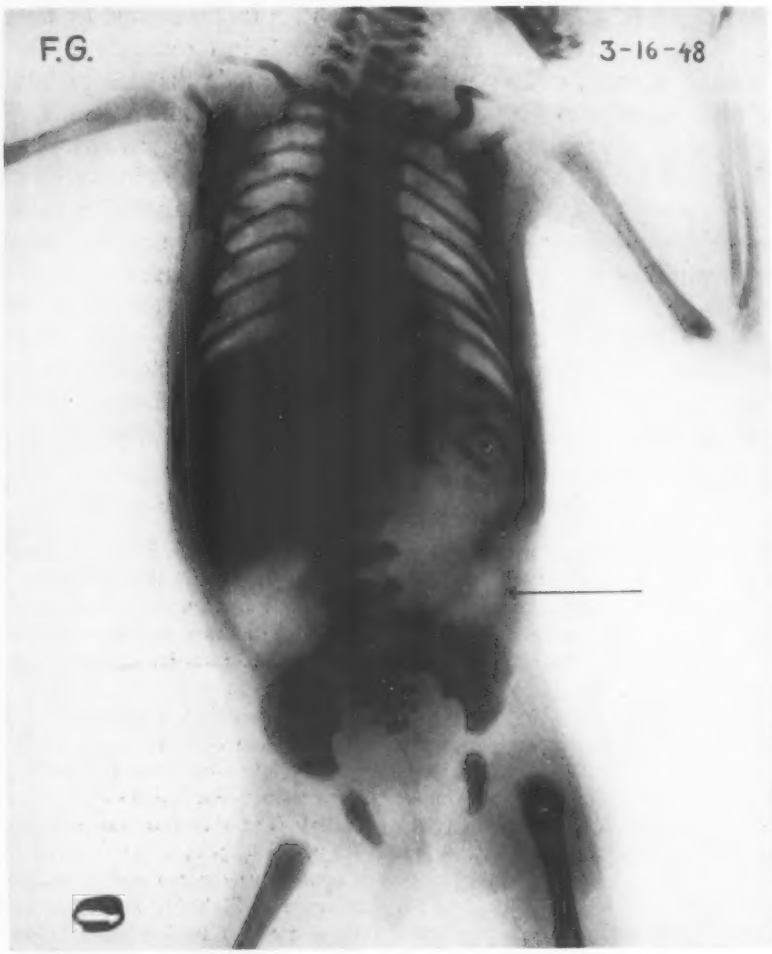

FIG. 1.—March 16, 1948; plain film of abdomen showing stomach, duodenum, and beginning of jejunum (arrow) markedly distended by gas. No gas is seen in remainder of intestine.

(March 16, 1948) revealed a large collection of air in the stomach, duodenum, and proximal few inches of jejunum. No gas was observed in the intestine distal to this (Fig. 1).

The appearance and clinical course were suggestive of high intestinal obstruction but because of the absence of abdominal distention or peristaltic waves and the apparent partial retention of gavage feedings and the passage of meconium stools, a thin barium mixture

was given by tube to corroborate the diagnosis. Meanwhile, hydration and supportive therapy were continued. The roentgenogram after barium administration showed passage of the mixture only as far as the first part of the jejunum (Fig. 2). The diagnosis of obstruction of the upper jejunum was now clear and efforts were made to prepare the infant for operation. By the following day (March 18, 1948) his condition was sufficiently improved to attempt surgery. The weight on this day was 3½ lbs.

FIG. 2.—March 17, 1948; Film after barium showing abrupt termination of barium column at proximal jejunum (arrow).

With a blood transfusion running and a gastric tube indwelling, laparotomy was performed (E. E. J.) The abdomen was opened through a right rectus muscle splitting incision. All the intestines were delivered. The large intestine was found to be incompletely rotated with the cecum subhepatic in location and the ascending and transverse

colon adherent to the transverse mesocolon and posterior peritoneum. These had to be dissected free before the pathologic condition responsible for the obstruction could be appreciated and exposed. After division of the adhesions and liberation of the colon, marked distention of the stomach, duodenum, and first portion of the jejunum was seen. This terminated about an inch beyond the ligament of Treitz in a blind pouch without continuity with the distal jejunum. Though tremendously dilated the bowel was viable. The distal blind jejunal end was located by tracing proximally from the ileocecal valve. The proximal segment of jejunum beyond the ligament of Treitz was too short to permit anastomosis. This technical difficulty was solved by reduction of the proximal segment through the fossa of Treitz, made possible by the blind termination. The distal bowel was so collapsed that its diameter was less than 0.5 cm. Its caliber was enlarged by distending it with saline and a two layer side-to-side jejuno-jejunostomy was then performed. Exploration revealed no further abnormalities. The wound was closed with interrupted figure-of-eight sutures of No. 32 stainless steel wire through fascia and peritoneum. The skin was closed with interrupted silk sutures.

The infant was replaced in the incubator with external heat and continuous oxygen. The gastric tube was left in situ. Penicillin was continued. During the first postoperative day the temperature rose to 102.4 degrees. The infant voided, and regurgitated small amounts of bile-stained fluid. Fluid requirements were met by hypodermoclysis. Twenty hours postoperatively small amounts of a 1:3 evaporated milk formula were fed through the indwelling tube. At this time the red blood count was 2,850,000 per cu. mm. and the hemoglobin 8.9 Gm. On the second day the baby retained about ½ ounce every 2 hours with occasional regurgitation of bile-stained fluid. Clyses were continued and a blood transfusion given. Twitching motions of the right arm and leg developed but responded to calcium therapy. Thirty-six hours after operation a formed yellow stool was passed which was strongly positive for occult blood, and thereafter about 3 to 4 yellow stools were passed daily. The infant's weight was 4 lbs. 2 ozs. on the seventh postoperative day. He gradually took larger and more concentrated feedings, with infrequent regurgitation. Repeated transfusions were given on the 2nd, 8th, 11th, and 33rd days for recurrent drops in hemoglobin. The icterus meanwhile had diminished so that it was only faintly appreciable.

Five weeks after the operation the infant was taking 2½ ounces of a strong formula. His weight at this time was 5½ lbs. The anterior fontanelle had opened and the sutures also seemed to be separating somewhat. The lesion in the right eye, according to the opinion of an ophthalmologist, was an embryoma. On May 7, 1948, 7 weeks after operation, the infant was discharged from the hospital weighing 6 lbs.

His development since has been progressive and, as far as can be made out, normal. On August 3, 1948, his weight was 10 lbs. 12 ozs. The head was seen to have grown proportionately to the rest of the body. The anterior fontanelle admitted a finger-tip and the skull sutures were palpable. The reflexes and reactions seemed within normal limits for the age. The wound was solidly healed and there were no digestive or bowel disturbances.

DISCUSSION

Atresia of the intestine may occur in the form of an internal diaphragm or, more commonly, the intestine ends as a blind sac discontinuous with the distal bowel or connected only by a fibrous strand. Multiple atresias, while less common, occur. Proximal to the obstruction the bowel is markedly distended; distally, it is very small and contains no gas. The cause is an arrest in development during the second or third month of fetal life when the bowel which has become filled with rapidly proliferating epithelium normally reestablishes its lumen.

The actual incidence of the lesion is difficult to appraise because of incomplete reporting and missed diagnoses. Without attempting to drain the literature, a few references will help to give an impression of the incidence. In 1922 Davis and Poynter collected 401 cases and added one. This figure included 134 atresias of the duodenum and 67 of the colon. Webb and Wangenstein in 1931 estimated the incidence of atresia and stenosis combined as about 1 to 20,000 infants. Including all the intestine below the pylorus and above the rectum, they found about 500 cases reported previously and added 13 cases of atresia and 4 of stenosis. Cohen in 1941 stated that since Webb and Wangenstein's paper at least 150 additional cases had been reported but they included all varieties of intestinal obstruction. In the same year Ladd and Gross reported 52 cases of intestinal atresia, only two of which were in the colon. Since 1941 individual cases or small series have been added by Duckett; by Glover, Smith and Eitzen; by Impink and Clammer; by Stock and Cannon; by Miller, Greengard, Raycraft and McFadden; by Erb and Smith; by Arnheim; by Biggs and Pontius; by Darne; by Judd, and others.

Symptoms usually begin on the first day of life. Vomiting is the presenting symptom. Persistent vomiting leads rapidly to severe dehydration. The vomitus almost always contains bile. The character of the vomitus will of course depend upon the level of the obstruction. While the stools may resemble normal meconium they are usually smaller and dryer. Farber's test which demonstrates the presence or absence of vernix cells in a stool specimen is of great usefulness in determining whether a complete obstruction exists. Abdominal distention may be present if the obstruction is low but may be difficult to evaluate if the atresia is high. Peristaltic waves crossing the abdomen may be seen but these are not constant.

A plain roentgenogram of the abdomen can give considerable information. No air is present in the intestine distal to the site of obstruction and if this be high, a dilated air-filled stomach, duodenum and upper jejunum with no air in the lower part of the field may establish the diagnosis. With ileal obstruction, multiple dilated loops with fluid levels are seen which are characteristic of intestinal obstruction but not necessarily of ileal atresia. Barium may be given to aid in the roentgen diagnosis but the danger of aspirating vomited barium accompanies such a procedure.

Surgical relief of the obstruction offers the only hope for survival. Otherwise, the markedly distended proximal blind loop undergoes necrosis, and perforation with peritonitis supervene. The procedure of choice is a side-tracking anastomosis. Naturally, resection of any nonviable bowel must be performed. Enterostomy should not be done as it always results in death due to rapid dehydration. Technically the operation presents certain difficulties due to the friability and distention of the proximal loop and the extreme narrow caliber of the distal. An excellent description of the technic may be found in Ladd and Gross.

Of equal importance to the operation is of course the pre- and postoperative handling of the infant. Fluid balance must be maintained and this is not an easy

procedure since it entails the administration of parenteral fluid several times a day. Blood and other supportive therapy must be utilized as indicated. A gastric tube should be introduced before the operation and should be continued after operation for as long as necessary. Operation should not be performed until the general condition has been brought to its best possible level even if this involves some delay. The infant frequently is not able to take feedings for several days after surgery and the stomach should be kept empty as long as vomiting persists. Feedings must be started carefully and increased judiciously. In all, the immediate period of postoperative care is one which requires painstaking and meticulous attention.

The mortality without operation is 100 per cent. According to Davis and Poynter, without operation death occurs after an average of 5 days when the obstruction is at the duodenal level as compared to 8 days at the colonic level. Even with surgery the mortality is quite high although it has lessened appreciably with modern techniques and improved preparation and postoperative care. The first recovery is credited to Fockens in 1911 who established a side-to-side anastomosis seven days after birth in a case of atresia at the junction of the middle and lower thirds of the small intestine. Of the 500 cases collected by Webb and Wangenstein only 10 recovered following surgery although the number operated upon is not given. Seven of Ladd and Gross' series of 52 cases treated surgically recovered. In Arnheim's report in 1945 he states that only 11 cases treated surgically to that date survived the procedure. While a number of individual successes have been added since then it is apparent that the mortality is still quite high.

The case reported here is of particular interest because it illustrates that even in a three and one-half pound premature infant a successful result may be achieved. The clinical picture and roentgen findings were typical of high jejunal atresia. The picture was complicated by the presence of icterus and other congenital defects were present in the form of closed fontanelles, an embryoma of the right eye, and an incompletely rotated colon. The last was not obstructing but required liberation and reduction before the primary pathology could be exposed and jejuno-jejunostomy performed.

SUMMARY

1. A case of jejunal atresia in a three and one-half pound premature infant, successfully treated by jejuno-jejunostomy, is presented.

2. Congenital intestinal atresia is briefly reviewed.

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MULTIPLE LIPOMAS OF THE STOMACH AND DUODENUM*

N. W. Fawcett, M.D., V. L. Bolton, M.D.,

AND

E. F. Geever, M.D.

Colorado Springs, Colo.

FROM THE DEPARTMENTS OF SURGERY, RADIOLOGY, AND PATHOLOGY OF ST. FRANCIS HOSPITAL, COLORADO SPRINGS, COLORADO

Less than 2 per cent of all surgically treated gastric tumors are benign, and among these about 3 per cent are lipomas. The incidence of benign tumors of the duodenum is considerably lower. In either region they may appear within the wall or as polypoid lesions. The symptoms are dependent on their location, size and character. A high percentage of benign tumors is symptomless and discovered only at autopsy. Not infrequently, however, the mucous membrane over a benign tumor ulcerates and produces symptoms of peptic ulcer, *i.e.*, pain and/or gastro-intestinal bleeding. Hemorrhage is sometimes massive. A benign tumor near the pylorus or in close relationship to the ampulla of Vater may produce symptoms of obstruction at these points. A pedunculated tumor, especially in the duodenum, may cause intermittent partial intussusception for the same reason that polyps of the jejunum and ileum may do so.

The case of a patient with an intramural lipoma of the stomach and intramural and polypoid lipomas of the duodenum is reported. The patient presented symptoms of hemorrhage and also intermittent episodes of pain.

M. B. S., a white male, age 36, was admitted to St. Francis Hospital March 30, 1948, because of recent gastro-intestinal hemorrhage. On admission gross bleeding had ceased and he was not feeling ill. His chief complaints on admission were: (1) Three episodes of tarry stools experienced in the past two years, accompanied by severe fatigue. The last episode occurred one week before admission to the hospital and was accompanied by faintness, palpitation and dyspnea. (2) Several episodes of vague abdominal discomfort accompanied by nausea during the past four years. He had consulted several different physicians for these attacks and the diagnosis was generally that of "probable appendicitis." However, the findings had never been definite enough to warrant surgical intervention.

The patient stated that the attacks of pain did not occur at the time of the tarry stools. Past and family history were irrelevant except that one child had been treated surgically for a Wilm's tumor.

Physical examination revealed a well developed, well nourished white male, apparently not acutely ill. General examination was negative throughout except for very slight tenderness to deep pressure just above the umbilicus. Laboratory studies including urinalysis, blood count, Kahn, blood sugar, N.P.N. serum amylase, and sedimentation rate were all non-contributory except that occult blood was present in the stool.

Roentgen-Ray Studies: A summary of the two examinations made showed a large filling defect in the stomach apparently projecting into the lumen although nothing could be palpated at the time of examination. The pylorus was not obstructed and the duodenal cap filled normally. Just distal to the cap was another large irregular deformity around

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which the barium seemed to flow, although again nothing could be palpated at the time. The stomach emptied normally in 5 hours.

On the basis of the roentgenologic findings the diagnosis rested between aberrant pancreatic tissue, a pancreatic tumor with secondary deformity of the stomach or the reverse. Other possibilities included leiomyomata, lipomata, and primary retroperitoneal growths such as Hodgkin's disease, or lymphosarcoma. Our final diagnosis was multiple tumors of undetermined type. Because of the patient's history of hemorrhage surgical exploration was advised.

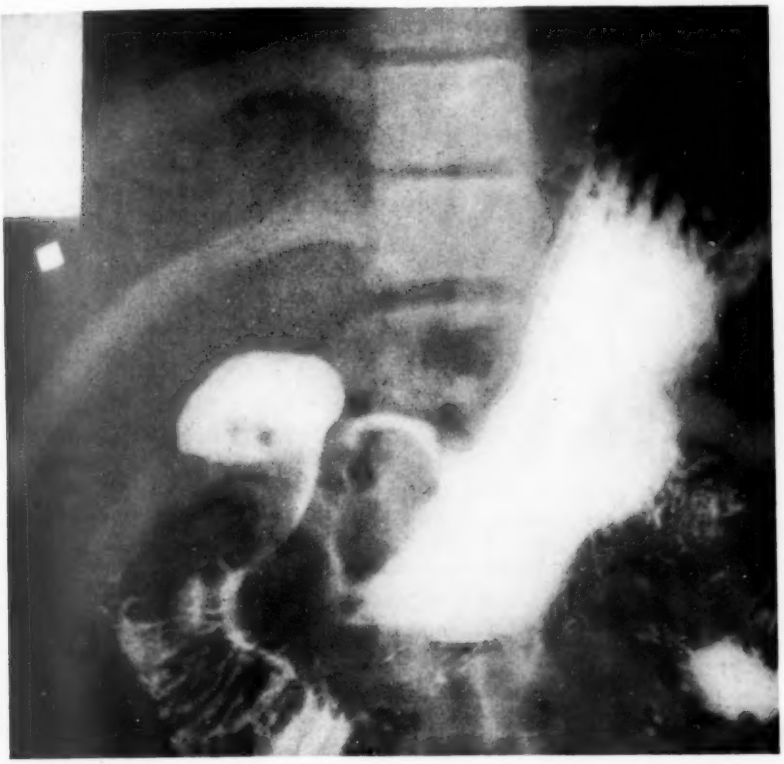

FIG. 1.—The antrum is contracting. The bulb is filled and the large irregular filling defect in the duodenal loop is visualized.

On April 2, 1948, the abdomen was explored through an upper transverse incision. Examination disclosed a large, soft, flat non-pedunculated tumor in the posterior wall of the stomach in the pre-pyloric region. A similar type of tumor occurred within the anterior wall of the second part of the duodenum, and upon opening the duodenum, it was apparent that a third tumor, which was pedunculated and arose from the mucosa at the lower border of the intramural tumor, projected down into the lumen of the third part of the duodenum.

Further exploration of the abdomen revealed no abnormal glands or other pathology. A subtotal gastrectomy and a resection of the anterior (tumor bearing) wall of the second portion of the duodenum was accomplished, re-establishing gastro-intestinal continuity by a retro-colic, Polya type, of gastro-jejunostomy.

Pathologic Examination. Stomach. Gross: The specimen consisted of the distal portion of the stomach and measured 13 cms. along the greater curvature. It had a max-

imum circumference of 16 cms. A thick, soft, intramural tumor, 9 x 8 x 3.5 cm. in dimensions, was palpable on the posterior wall. The overlying mucous membrane was smooth and contrasted strikingly with the prominent, greyish-red, rugal folds elsewhere. (Fig. 2 upper specimen.) The cut surface of the tumor revealed lobulated and bright yellow fat which was mainly submucosal in distribution. Microscopic examination showed that the tumor was composed mainly of mature fat cells. Focal congestion, fibrosis and round cells were scattered throughout.

Duodenum: Gross pathologic specimen consisted of the anterior portion of the wall of the second part of the duodenum and measured 5 x 3 cm. in surface area. A thick, soft, intramural tumor measuring 4 x 3.5 x 1.7 cm. was palpated. A similar polypoid tumor covered by ulcerated and purplish red congested mucous membrane projected from the mucous membrane surface of the main specimen. The polyp projected into the lumen towards the third part of the duodenum. The polyp measured 7 cm. in length and 3 x 3 cm. in cross section. Two stellate shaped ulcers were apparent in the midportion of the polyp. The largest ulcer measured 1.5 x 2.2 cm. in area. (Fig. 2 lower specimen.) The cut surface of the tumor was lobulated and bright yellow, similar to that described in the stomach. Microscopic examination showed moderate congestion and hemorrhage of the mucous membrane over the polypoid lesion. The base of the ulcer described grossly was composed of proliferating and congested capillaries, fibroblasts and scattered polymorphs.

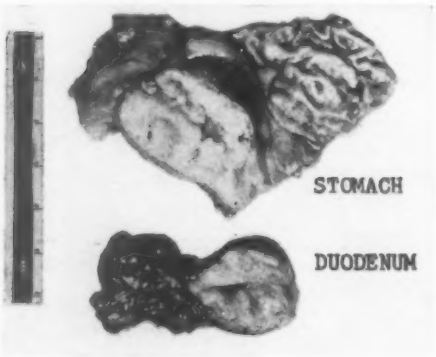

FIG. 2.—Cut surfaces showing lobulated fatty character of the intramural tumors.

Pathologic diagnosis: Lipomas, stomach and doudenum, polypoid in the latter region and associated with secondary ulceration.

Postoperative course was uneventful and he was discharged on April 20, 1948.

DISCUSSION

The preoperative diagnosis of these lesions, if made, is usually made by the roentgenologist. However, in the roentgen diagnosis of benign lesions of the stomach or duodenum it is difficult to determine with any degree of accuracy the histologic nature of the growth. Since these tumors are so unusual, no one has acquired a very extensive experience with them.

However, there are features which aid in the differentiation between benign growths and ulcers or malignant deformity. Most of these tumors grow into the lumen so that they tend to produce a smooth rounded filling defect. Since they are not invasive, the borders, in general, are well demarcated but with obliteration of mucosal pattern. The peristalsis is not greatly affected, if at all. Therefore, emptying time is not influenced unless there is obstruction and, consequently, little or no change in the size of the stomach or duodenum is noted. The growth will move with the stomach on palpation during fluoroscopy and the stomach or duodenum will not be displaced as would be the case with extrinsic masses. Lipomas seem particularly prone to ulcerate so that one may be able to locate a crater, especially on second examination or with the "advantage of hindsight."

SUMMARY

A case of multiple lipomas of stomach and duodenum is presented in a 36-year-old white male. The tumors in the duodenum were in part polypoid and complicated by ulceration of the overlying mucosa. His symptoms were: Gastro-intestinal bleeding and episodes of pain. Subtotal gastrectomy and duodenectomy and retro-colic, Polya type, gastro-jejunostomy were performed. The postoperative course was uneventful.

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ANOMALOUS INSERTION OF THE RIGHT HEPATIC DUCT INTO THE CYSTIC DUCT*

REPORT OF A CASE AND REVIEW OF THE LITERATURE

MATHEW W. KOBAK, M.D., AND RALPH B. BETTMAN, M.D.

CHICAGO, ILL.

FROM THE DEPARTMENT OF SURGERY, MICHAEL REESE HOSPITAL, CHICAGO

ANOMALIES OF THE BILIARY DUCT SYSTEM are not infrequent and are of vast importance in adequate assessment of the technic of cholecystectomy. Kehr[1] in pointing out the high incidence of morbidity and mortality entailed early in his series observed that, in the majority of cases, this could be directly traced to anomalies in the biliary duct or vascular system. Eisendrath[2] similarly emphasized the necessity of adequate knowledge of the anomalies that might be encountered in the course of what might otherwise be routine cholecystectomy. In more recent years Graham *et al.*[3] and Daseler *et al.*[4] have also served warning of the variations that might be found in dissection of the cholecysto-duodenal ligament, and it is now common knowledge that anomalies must be constantly watched for in the performance of surgery in this region of the body.

Recently during a cholecystectomy performed by one of us (RBB) an unusual anomaly was encountered, the right hepatic duct draining into the cystic duct (Fig. 1). Because of the reputed rarity of this anatomic condition and its surgical hazard if not recognized, it is deemed timely to report this case.

CASE REPORT

The patient, a 42-year-old white male was admitted to Michael Reese Hospital with a typical history and diagnostic findings of gallbladder disease. A cholecystectomy was therefore performed, and dissection of the cholecysto-duodenal ligament conducted in the usual manner previously described by this clinic.[5] What were thought to be the hepatic, cystic and common ducts were carefully identified and these along with the vascular structures dissected free. At this time, on close observation, it was noted that the duct system was anomalous, the right hepatic duct draining into the cystic immediately below the gallbladder. As a result it was necessary to clamp the cystic duct above the union with the right hepatic in order that the right hepatic might drain freely into the common duct. Cholecystectomy was then performed from below upward, and the patient's postoperative course was uncomplicated.

DISCUSSION

Anomalous insertion of the right hepatic duct into the cystic, or of the cystic into the right hepatic has been observed in both animals and man. Boyden[6] in the course of thousands of dissections of domestic animals noted this condition in a number of instances as indicated by his anatomic drawings. Similarly Thompson[7] and Daseler *et al.*[4] observed examples of this condition in the dissection of cadaver material.

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Embryologically it would seem that this phenomenon could best be explained by variation in growth of the hepatic diverticulum in its formation of the biliary duct system. This outgrowth of the foregut in its primary division forms the common duct, and the branchings therefrom the cystic duct and gallbladder, and the hepatic duct. The germination of the hepatic duct then branches to form the right and left hepatic duct system in its secondary rami-

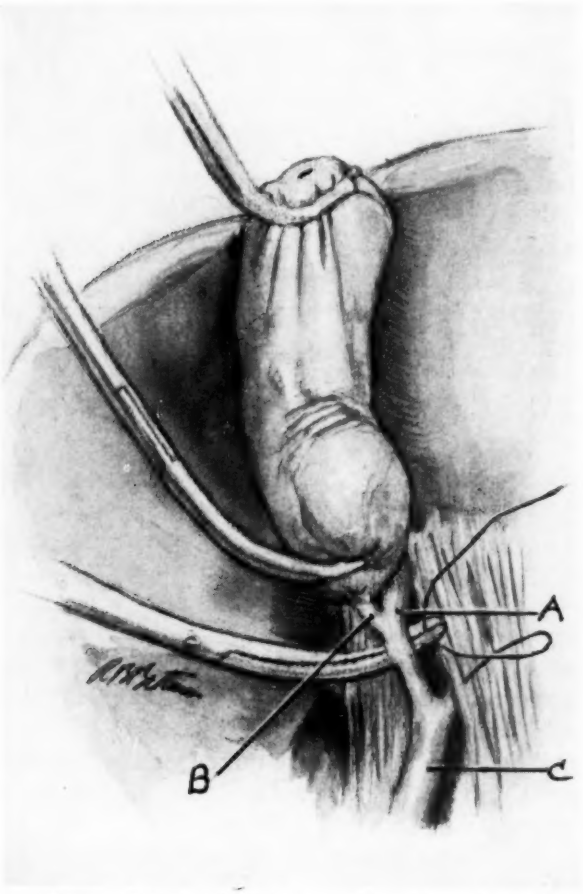

FIG. 1.—Illustrating the anomalous insertion of the right hepatic into the cystic duct, and how this duct might inadvertently be ligated. (a) Right hepatic duct. (b) Cystic duct. (c) Common duct.

fications. An anomaly of the right hepatic entering the cystic could thus occur if an abnormality of the cystic duct bud extended into the liver substance. At the same time it would be necessary that the primary hepatic diverticulum failed to divide, and thus only formed the left hepatic duct.

Another possible explanation of the derivation of this anomalous situation could be found in unusual absorption of the many small secondary branchings

which project from the various buddings of the hepatic diverticulum. Leiter[8] has suggested the additional possibility of an early branching of the primary duodenal bud into right, left and cystic ducts, with the cystic originating so far down as to arise from the right hepatic duct.

From the studies of Thompson,[7] Daseler *et al.*[4] and from those[2, 9-16] in which this anomaly was not found, it is possible to obtain a reasonable estimate of the incidence of the finding. These results as tabulated (Table I) show that in the course of 1371 cadaver dissections of the biliary tract, anomalous right hepatic-cystic duct union has been encountered only four times.

If one were to judge the relative importance of the problem by the above data it would not be a cause of great concern to any individual operator. However in view of the great number of cholecystectomies performed each year it

TABLE I.—*The Incidence of Right Hepatic-Cystic Duct Union Encountered in Cadaver Dissections.*

Author	Year	Number of Dissections	Number of Times Anomaly Found
Brewer	1900	100	0
Ruge	1908	50	0
Descomps and De Lalaubie	1910	50	0
Piquand	1910	40	0
Eisendrath	1920	100	0
Flint	1923	200	0
Beaver	1929	57	0
Thompson	1933	50	1
Lurje	1937	194	0
Osler	1945	30	0
Daseler *et al*	1947	500	3
Total	....	1371	4

would seem that this surgical anomaly calls for greater awareness on the part of the general population of physicians. That the calculated low incidence of 0.29 percent might be small may be concluded from the series of Daseler *et al.*, the most recent of the dissections, where three instances of this anomaly were found in 500 cases. Also in the prior dissection of Thompson one case was revealed in fifty examinations.

Strangely in the course of surgery the condition has not been reported frequently. Considering the expected incidence based on anatomic dissections the fact that only two cases could be discovered in a reasonably complete search of the literature would seemingly imply that either surgical dissections have been incomplete, or that the postoperative complications resulting from the anomaly were not sufficient to warrant further search for their causes.

In Kehr's case[1] calculi lying in the right hepatic duct were thought to be in a diverticulum of the cystic duct. As a result, the hepatic duct was divided and had to be anastomosed to the common duct. In Leiter's case[8] it was necessary to divide the hepatic ducts in order to remove a tumor of the ducts. The anomaly was observed in the course of the dissection. In this case the hepatic ducts were anastomosed separately to the duodenum. Both these patients did

well postoperatively. In the present instance anastomosis of the duct was not necessary, the cystic duct having been tied off carefully above the junction with the hepatic.

Insofar as complications might be expected, it would seem that two would be probable. These would stem either from obstructing the flow of the right hepatic duct by ligature (Fig. 1), or by failing to recognize the situation and leaving a draining right hepatic duct after removing the cystic duct along with a portion of the right hepatic.

From the fact that autopsy reports have not noted the finding of these complications, it would appear that either the anomaly has been recognized, the complications corrected, or else that by themselves, these complications need not prove fatal. This would seem to be a feasible explanation in experimental situations where the right hepatic duct was ligated. In some of the animals so treated it has been observed that collateral channels will shortly allow bile to flow from the right lobe of the liver through the left hepatic duct. Fortunately the reserve of the liver is great and the left lobe apparently is capable of adequately handling the increased load. Clinically, though, there could be little doubt but that in such instances the general status of patients would be poorer over the immediate postoperative period.

In those instances where the right hepatic duct has been severed, the possibility of biliary fistula, or bile peritonitis, would be of greater import. However, bile flow from the severed duct renders this condition relatively easy of recognition.

Treatment of the complications depends on immediate cognizance of the anomaly with prompt repair of the damaged duct. It is, however, appropriate to emphasize that the most important aspect of therapy lies in the field of prevention. Here the prime factors are recognition of the fact that anomalies are not infrequent in large series of cases, and that a knowledge of these is essential. If the morbidity and mortality of cholecystectomy is to be lowered, continued vigil is necessary at the operating table in order to recognize anomalies existing in the hepatic pedicle.

SUMMARY

A case of a rare anomaly of the biliary duct system has been reported. In this instance the right hepatic duct joined the cystic duct just below its emergence from the gallbladder. The cystic duct eventually united with the left hepatic to form the common duct. The literature bearing on the subject has been reviewed and the embryology, incidence, complications and treatment discussed.

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PRIMARY INFLAMMATION OF THE APPENDICES EPIPLOICAE*

WITH REVIEW OF THE LITERATURE AND REPORT OF SIX ADDITIONAL CASES

T. P. Marinis, M.D., and J. H. Cheek, M.D.

Dallas, Texas

FROM DEPARTMENT OF SURGERY, BAYLOR UNIVERSITY HOSPITAL, DALLAS, TEXAS

Since the first description of appendices epiploicae some 400 years ago interest in them as sites of primary disease has recurred from time to time. Scattered individual cases have been reported in which they have been found free in the peritoneal cavity or in which some primary pathologic process has caused surgical intervention. Interest has been stimulated by the excellent reviews of Hunt,[1] Klingenstein,[2] Fiske[3] and more recently by Pines,[4] but recognition of primary disease of the appendices epiploicae is still rare.

Primary disease of the appendices epiploicae has attracted attention only by its rarity and this continues to be true in spite of the fact that it occurs more frequently than is implied by the infrequency of reports. We feel that it is timely to call attention to primary disease of the appendix epiploica and to present a review of the available literature, bringing the cases up to date and to add six additional cases. In this report we have gathered, and are presenting, only cases in which primary disease of the appendix epiploica have produced acute symptoms and signs which have warranted surgical exploration.

ANATOMY AND PHYSIOLOGY

The anatomy and function of appendices epiploicae should be mentioned. They have been shown to be present as early as the fifth fetal month. They occur along the large bowel except in the region of the rectum, and may have one to three rows though only one or two are usually demonstrated. They are definite fat tabs of irregular shape which are continuous with the subserosal fat layer and are enveloped by a layer of the visceral peritoneum from the large bowel. Their blood supply is gained from one artery and vein from either the superior or inferior mesenteric vessels.

The significance of these structures is obscure and their physiologic function has never been proven but the idea that they play a role in the absorption of fluids and as a protective mechanism for the colon seems justified. This latter may be in protection from other inflammatory processes or from adjacent viscera during peristalsis. Pines[4] felt that appendices epiploicae acted as protective fat pockets for the redundant intestinal vessels and that this protective mechanism was obviously necessary to prevent collapse and occlusion of the vessels when the bowel became distended. It should be further added that in all probability they have a definite role in the storage of fat.

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PATHOLOGY

The etiology of primary disease within the appendices epiploicae has been discussed by many correspondents.[2, 3, 5, 6, 7] The consensus of opinions is that torsion of the pedicle is usually the direct cause in spite of the fact that in many cases it cannot be demonstrated. It seems reasonable that it is the principal cause of interference of the blood supply, and is due to a variety of conditions, such as movement in adjacent coils of small bowel during vigorous peristalsis and the association of a large appendix epiploica with a long pedicle. Infarction may be present and has suggested, when torsion was not demonstrated, that it is due to thrombosis or embolism.[4, 5] Payr[8] thought that engorgement could be due to an abnormally long vein becoming twisted about the artery. Secondary changes which may occur include simple necrosis, various degenerative processes and gangrene. Why they should be the site of a primary inflammatory process has never been explained, though it is obvious when associated with other inflammatory lesions within the abdomen. Black[9] was the first to suggest that they could be the site for developing lipomas.

ANALYSIS OF CASES PREVIOUSLY REPORTED

Fifty-eight cases have been previously reviewed or reported in the literature in which the symptoms and signs were of an acute or subacute abdominal disease and subsequently required surgery. This does not include cases which appeared to have had a chronic course over months or years, cases in which the appendices epiploicae were found in hernial sacs, noted at autopsy, cases associated with other inflammatory processes, or cases in which they were found incidentally at surgery for some other disease.

The site of the diseased appendix epiploca was on the sigmoid colon in 28 cases and on the cecum in 13 cases. The others occurred on various parts of the remaining colon. Torsion of the appendix epiploica was the most frequent diagnosis given, though in a majority of the cases the findings were not described. Thirty-six of the cases occurred in males and 22 in females. The ages ranged from 18 to 76 years with a majority (31 cases) occurring between 30 and 50 years. The symptoms and signs were incomplete in many cases; however, all cases had pain and it appears to be the only constant finding. In 46 cases tenderness was present and was most commonly seen overlying the diseased appendage. Nausea, vomiting or both occurred about as frequently as rigidity, that is, in about one-half of the cases. Rebound tenderness and a mass were only occasional findings.

REPORT OF ADDITIONAL CASES

Case 1.—A 40-year-old white male was admitted to the hospital with a history of gradual onset of lower abdominal pain 48 hours before which increased in severity and moved to right lower quadrant 24 hours prior to admission. He had a constant desire to defecate after onset. No nausea or vomiting was associated. He had had a previous similar attack 13 years ago lasting 24 hours. Examination revealed temperature of 98.6, WBC was 7,050. He exhibited moderate tenderness and well marked rigidity in right lower quadrant with no rebound tenderness. Preoperative diagnosis of acute appendicitis was made. At operation a large amount of bloody fluid was found and a gangrenous

appendix epiploica of the sigmoid measuring 6 x 4 cm. was present and removed. Postoperative course was uneventful.

Case 2.—A 47-year-old female was admitted to the hospital with a history of sudden gripping pain in the midline, above the symphysis for 12 hours previously. The pain "went through to the back." She had anorexia, but no nausea or vomiting. The pain moved to the lower left quadrant, back to midline and then to right lower quadrant. There was an urge to defecate with results. Examination revealed moderate tenderness over right lower quadrant with rebound tenderness to the same side. This tenderness shifted with position of the patient, from right lower quadrant to midline to left lower quadrant and back to right lower quadrant. Pelvic examination revealed tenderness in the right cul-de-sac. The temperature was 99.4, WBC 11,700. Preoperative diagnosis was acute appendicitis. At operation there was found a swollen blue appendix epiploica attached to the sigmoid, which was removed. Postoperative course was uneventful.

Case 3.—A 32-year-old female was admitted to the hospital with a history of fullness and discomfort in abdomen for 48 hours becoming painful and moving to right lower quadrant. This was not relieved by enemas or rest in bed as previous attacks had been. There was no nausea or vomiting. Moderately severe pain in right lower quadrant persisted. Examination revealed the temperature to be 99.0 and WBC 12,400. Moderate tenderness in right lower quadrant was present with no rebound tenderness and no masses. Preoperative diagnosis was acute appendicitis. At operation a blue gangrenous appendage was found in the pelvis which was attached to the sigmoid. It was removed and the postoperative course uneventful.

Case 4.—A 19-year-old white female entered the hospital for change of cast and further treatment for old fracture of right femur. While in the hospital she had onset of severe cramping abdominal pain which was followed by nausea and vomiting. Pain became more intense and was localized in the right lower quadrant with marked tenderness in same area. Temperature was 99.6 and WBC 14,100. Preoperative diagnosis was acute appendicitis. At operation the appendix was found to be normal and attached to cecum was an enlarged gangrenous appendix epiploica which was removed. The postoperative course was uneventful.

Case 5.—A 44-year-old male was admitted to the hospital with a history of slight epigastric pain and dysphagia of 72 hours duration, followed by severe right lower quadrant pain associated with nausea and vomiting. Examination revealed marked tenderness in the right lower quadrant. No masses were felt. The temperature was 100 and WBC 12,500. Preoperative diagnosis was acute appendicitis. At operation a dark gangrenous appendix epiploica measuring 5 x 0.8 cm. attached to the cecum was found. It was removed and postoperative course was uneventful.

Case 6.—A 34-year-old male was admitted to the hospital with a history of onset of abdominal pain 24 hours previously which had moved to the right lower quadrant and was noticed more when moving about. No nausea or vomiting was associated. He was admitted for a stat appendectomy. Examination revealed temperature of 98.6 and WBC 12,900. Marked tenderness in right lower quadrant was present with rebound tenderness. No masses were palpable. Preoperative diagnosis was acute appendicitis. At operation there was found an enlarged gangrenous appendix epiploica attached to the lower ascending colon. It was removed and postoperative course was uneventful.

DISCUSSION

In Baylor Hospital during the last 10-year period there have been six cases of primary disease of the appendices epiploicae producing symptoms sufficient

to cause surgical exploration. Within this same period of time it is of interest that surgery was done in 2766 cases for acute appendicitis. Also during this period primary disease of an appendix epiploica was found at time of surgery for some other disease process in four instances, yet no history could be obtained of any symptoms which they might have produced.

In the cases we are reporting symptoms were present for 48 hours or less except in one case of 72 hours duration. In four cases onset of pain was localized to the right lower quadrant. In others it was generalized or in the lower abdomen. Nausea and vomiting was present in three cases. In all cases tenderness was moderate to marked and localized to the right lower quadrant. Of considerable interest was the one case in which the tenderness was shifting in character. Rigidity and rebound tenderness was present in three cases each. Low grade temperature elevation was noted in three cases and an elevated WBC count was present in all except one. Torsion was not demonstrated in any of these cases.

We feel that we are justified in only presenting cases associated with symptoms of acute disease and which have required surgical intervention. Though torsion of the pedicle of the appendix epiploica is apparently the most likely cause of disorder, we were unable to show it in any of these cases. We feel that the sign of shifting tenderness should cause one to suspect the condition and want to stress again that in any acute surgical abdomen in which primary disease cannot be demonstrated elsewhere one should explore thoroughly for the presence of a diseased appendix epiploica.

It is quite apparent that pathologic changes may occur in the appendices epiploicae without producing symptoms and this most likely accounts for those found incidentally at other operations and at autopsy. It is just as apparent that in many instances these do produce symptoms and signs of an acute abdominal disease and in such cases surgical exploration is indicated.

SUMMARY

The available literature has been reviewed and the cases of primary disease of the appendix epiploica unassociated with other conditions or which were found incidentally, have been collected and brought up to date. To this number we are adding six cases in which the primary disease justified surgery. We have suggested that shifting tenderness should cause one to suspect the disease, and in all cases of acute abdomens in which a primary disease is not found one should look for a diseased appendix epiploica.

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Editorial Address

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY.

John H. Gibbon, Jr., M.D.

1025 Walnut Street, Philadelphia 5, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to Dr. Gibbon at the above address.

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ANNALS OF SURGERY

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ANGIOSARCOMA OF THE COLON*†

WITH CASE REPORT

CHARLES A. STEINER, M.D., F.A.C.S.
AND
LOUIS H. PALMER, M.D.
UPPER DARBY, PA.

THE RARITY OF SARCOMA of the colon is stressed in every treatise on this subject. This condition was first described by A. Debruner[1] in 1883, prior to which time it is likely that it was not recognized by the pathologists as a distinct disease entity. Subsequently additional cases were reported by Jopson and White,[2] Farr[3] and others,[4, 5, 6, 7, 8] but in a rather careful review of the literature, we have been able to find less than 400 proven cases. Furthermore, of these cases, approximately 95 per cent are lymphosarcomas. In view of the rarity of all types of sarcoma of the colon, we feel that a case report of an angiosarcoma would be of value, particularly since we are unable to find any description of such a neoplasm in the literature.

Although an adequate description of nearly all types of sarcoma of the colon is readily available through numerous sources, very little has been written about angiosarcomas arising in any part of the body, and as stated above, no previous description is obtainable of an angiosarcoma of the colon. However, it is felt that this lesion is an extremely vascular neoplasm which arises from the cells of the outer coat of a blood vessel and it is not considered to be a very highly malignant tumor. A further description of this lesion is incorporated in the following case report.

CASE REPORT

Mrs. H. F., a 46-year-old white female, was admitted to the Bryn Mawr Hospital on November 27, 1945, with a chief complaint of abdominal pain of three days duration. She had apparently been perfectly well until November 24th, at which time she developed a colicky type pain in the left lower quadrant of her abdomen several hours after taking a laxative. Later in the day, the pain increased in severity and was not relieved by an enema. On the following morning she became nauseated, vomited several times and noticed that her abdomen was becoming distended. Further laxatives and enemas during the next 48 hours were ineffectual, at the end of which time her abdomen was considerably distended and the patient was obviously quite ill. She was then admitted to the Bryn Mawr Hospital for further observation.

The past medical history in this case was essentially negative, there having been no serious illnesses or operations. There had been no weight loss and no symptoms referable to her gastro-intestinal tract. Her menstrual history was likewise negative.

Physical examination revealed a rather pale, somewhat obese, white female. Blood pressure was 130/80, temperature 99.2°F., pulse 88, respirations 22. No abnormalities except the following: rather marked distention of the abdomen with considerable tender-

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ness in the left lower quadrant, an ill defined boggy mass was palpable at this point. Peristalsis was hypo-active. Rectal examination was negative.

Roentgenologic examination by means of an erect scout film showed the large bowel to be moderately distended proximal to the sigmoid colon.

Immediate treatment consisted of the administration of parenteral fluids and the passage of a Miller-Abbott tube, as a result of which the patient's condition improved quickly and the abdominal distention was relieved in 48 hours. A barium enema thereafter revealed a partial obstruction at the junction of the descending and sigmoid colons. The Miller-Abbott tube was removed and the patient was placed on a

FIG. 1.—Gross specimen angiosarcoma of sigmoid colon.

regimen of sulfasuxidine, parenteral feedings of glucose, saline and blood plasma together with a low residue, high protein diet. Operation was performed on December 5, 1945, eight days following admission.

Operation. With continuous procaine spinal anesthesia, the abdomen was opened through a left lower paramedian incision and exploration revealed a firm nodular type growth in the wall of the sigmoid. The serosa of the involved area of bowel was smooth and glistening in appearance. No enlarged lymph nodes were palpable in the mesocolon nor in the retroperitoneal tissues and no gross invasion of surrounding

structures was noted. Similarly, no evidence of metastasis to the liver was present. No abnormalities of the pelvic organs could be detected. Resection of approximately 10 cm. of the sigmoid colon together with a large wedge shaped piece of mesocolon was performed, followed by an open end-to-end anastomosis. Five grams of sulfanilamide crystals were placed in the abdominal cavity following which the incision was closed in layers without drainage. A tentative diagnosis of carcinoma of the colon was made. Five hundred cubic centimeters of whole blood were administered during operation and the patient's immediate postoperative condition was good.

Postoperative Course. Continuous nasal suction with the use of a Levin tube was carried out for the first two postoperative days together with parenteral feedings of glucose in saline and blood plasma. Ambulation was instituted on the first postoperative day. Oral feedings were begun on the third day and at the end of ten days the patient was eating a full high protein, low residue diet and was having regular bowel movements without laxatives. Her incision healed by primary intention and she was discharged from the hospital on December 20, her 15th postoperative day.

Pathologic Report of Specimen (By Dr. Max M. Strumia, Pathologist to the Bryn Mawr Hospital).

Gross Description: (See Figure 1) Section of colon measuring 10 cm. in length and 2½ cm. in diameter with numerous fatty appendages. On the external surface are two cyst-like polypoid growths about 2 cm. in diameter, side by side; one appears to be filled with dark red material and the other with dark yellow material. On cut section, there is annular thickening and constriction in the wall of the gut 3½ cm. in diameter. Growing from this constriction are numerous polypoid masses.

Microscopic Description. (See Figure 2) (1) Generally well preserved mucosa overlying a nodular mass of atypical tissue consisting of broad interlacing bundles of spindle cells, often with fibrillar differentiation, fairly ev[illegible] in morphology with a moderate number of mitotic figures. Certain portions of the tumor contain a very large number of vascular spaces generally without lining. (2) Similar to (1) except that it contains a large nodular mass in which large vessels exist which have a definite wall. (3) Similar to proceeding ones, but shows a myxomatous degeneration of the tumor.

Pathologic Diagnosis. Hemangiosarcoma of colon, vascular (angiosarcoma).

In view of the unusual nature of this tumor, Doctor Strumia presented the slides to a number of his colleagues at a Pathological Conference at the University of Pennsylvania, Philadelphia, Pennsylvania, and they agreed with his interpretation.

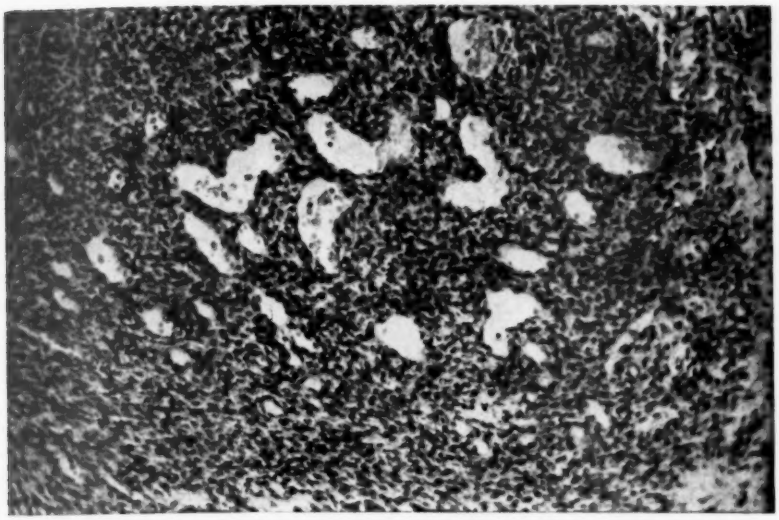
Subsequent Course to Date. This patient was next seen on January 25, 1946, for a routine follow-up examination. At this time she had gained weight, was eating well and had no gastro-intestinal complaints. She did mention, however, that she was experiencing metrorrhagia and a gynecologic consultation was advised.

It was not until July 15, 1946, however, that the patient first consulted Dr. Mario A. Castallo for gynecologic examination. At this time, the uterus was found to be the size of a three months' gestation with a large polypoid growth extending from the cervical os to the posterior vaginal vault. On July 23rd, dilitation and curettage and cauterization of the cervix with removal of the polypoid mass, followed by the insertion of 3600 mg. hours of radium in the cervical canal, was done by Doctor Castallo at St. Mary's Hospital, Philadelphia, Pennsylvania.

Microscopic sections of this polyp revealed it to be of a sarcomatous nature closely resembling the primary tumor of the colon. (See Figure 3)

The patient was then sent to Dr. Paul Eberhard at Jefferson Hospital for roentgen-ray therapy. On September 26, 1946, roentgen-ray therapy was started to two anterior and two posterior pelvic ports, and 2000 r were delivered to each port. Another 3000 r was given directly to the original site of the lesion through an intravaginal cone. At the conclusion of this treatment, all evidence of the original lesion had completely disappeared and

FIG. 2



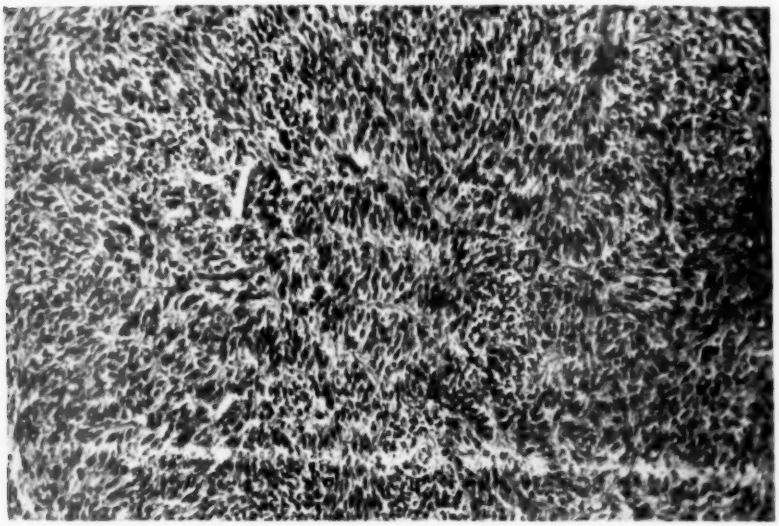


FIG. 3

FIG. 2.—Microscopic section angiosarcoma of sigmoid colon.
FIG. 3.—Microscopic section of sarcomatous uterine polyp.

vaginal examination by Doctor Castallo on October 11, 1946, revealed the uterus to be smaller in size with no evidence of recurrence of the polypoid mass.

The patient was last seen in September of 1947, at which time examination was entirely negative and the patient was symptom-free.

SUMMARY AND CONCLUSIONS

I. Less than 400 proven cases of sarcoma of the colon have been described in the literature, and of these, approximately 95 per cent are lymphosarcomas.

II. A case of angiosarcoma of the colon is presented which we believe is the first to be described.

III. In the two and a half year interval since resection of the neoplasm, this patient has had no symptoms referrable to her gastro-intestinal tract. She did develop, however, a uterine polyp which upon removal was found to be of a sarcomatous nature, closely resembling the primary tumor of the colon. The relationship between this lesion and that of the sigmoid colon is open to conjecture.

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ANNOUNCEMENT

The Buffalo Surgical Society announces the award of the Roswell Park Medal to Dr. Evarts A. Graham for outstanding surgical achievement.

Doctor Graham will give the Roswell Park lecture May 5, 1949, at the Kleinhans Music Hall, 9:00 P. M., Buffalo, N. Y.

BOOK REVIEW

DETAILED ATLAS OF THE HEAD AND NECK by R. C. Truex and C. E. Kellner. New York, 1948, Oxford University Press.

This superb work was designed to supply the needs of students and practitioners alike, who are interested in regional anatomy of the head and neck. It contains original presentations of clearly identified structures arranged in "layers" from without inwards, frontal and transverse sections, skeletal structures, and a large section on cerebral anatomy. In contrast to other recently published atlases for use in special fields of head and neck surgery, this volume is all inclusive. Small scale drawings of detailed anatomy of the orbit, jaw, larynx, etc., have been prepared with a view toward clinical application, and the specialist in any field of this part of the body will find them well worth while. Cadavers were specially dissected for the illustrations. Original drawings in each series were made from the same specimen for uniformity of scale. In those instances where the scale was altered, that fact is accurately noted.

The student, especially in his first medical school year, will benefit by using this atlas as a supplement to his major text book. As indicated in the introduction by E. A. Boyden, the change in emphasis from systemic to regional study of anatomy reflects an "awareness of the inextricable relation between the basic medical sciences and their clinical applications."

HENRY P. ROYSTER, M.D., Philadelphia.

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LETTER TO THE EDITOR

DEAR SIR:

The National Paraplegia Foundation wishes to announce the establishment of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of $3000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships will be awarded by the Medical Advisory Committee and are open for award for the academic year 1949–1950. Application forms may be obtained from the Chairman of the Medical Advisory Committee, and applications should be submitted to him not later than June 1, 1949.

L. W. Freeman, M.D.
Chairman, Medical Advisory Committee
National Paraplegia Foundation
1040–1232 West Michigan Street
Indianapolis 7, Indiana.